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PROCEEDINGS

of the

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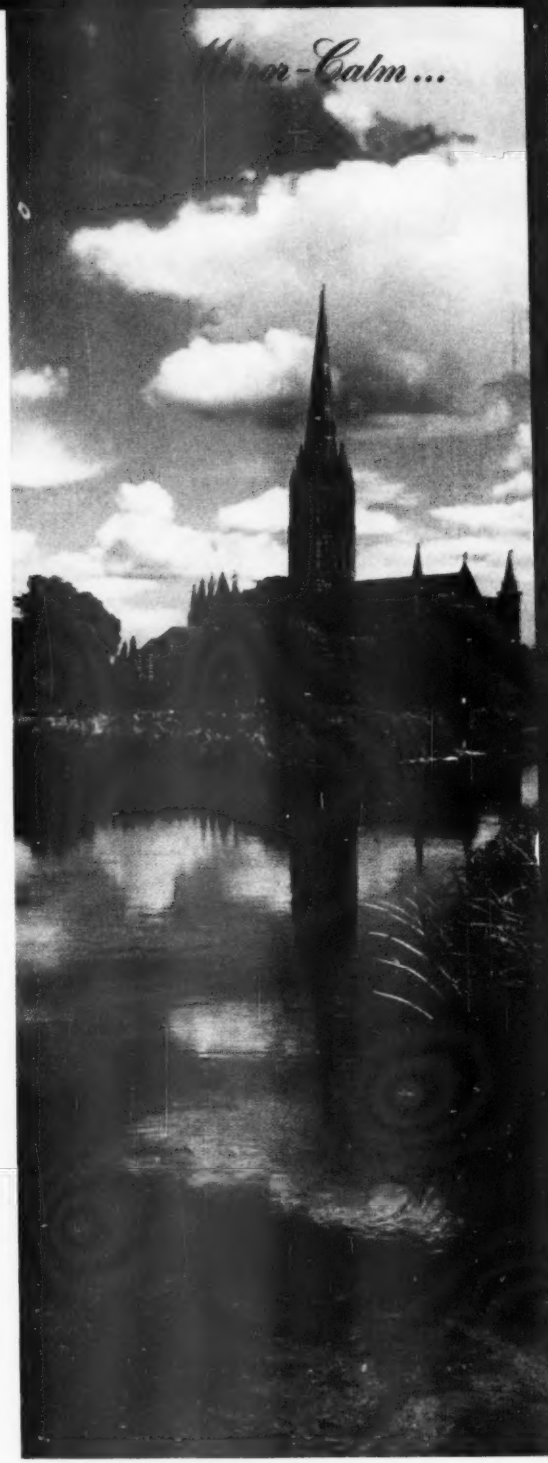

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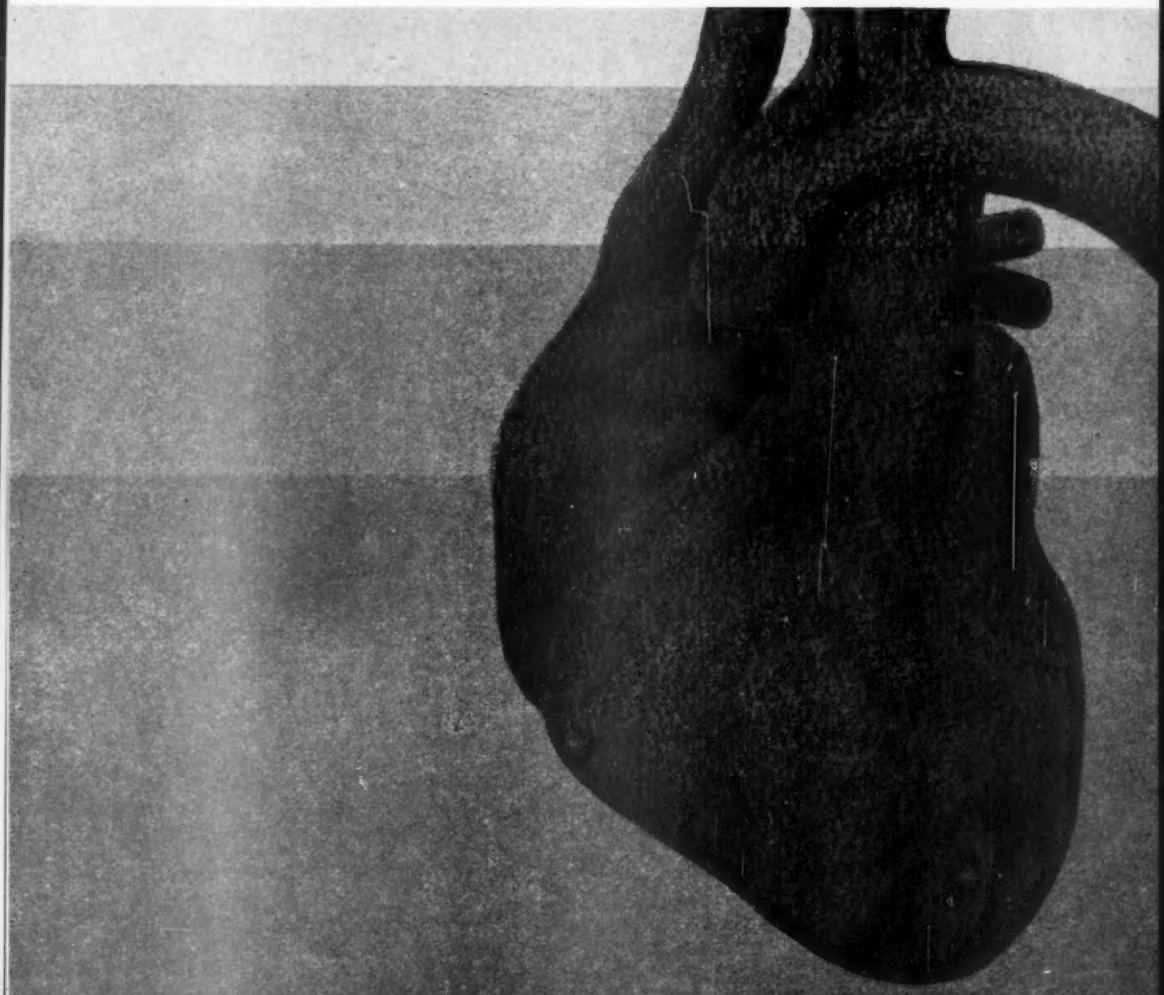

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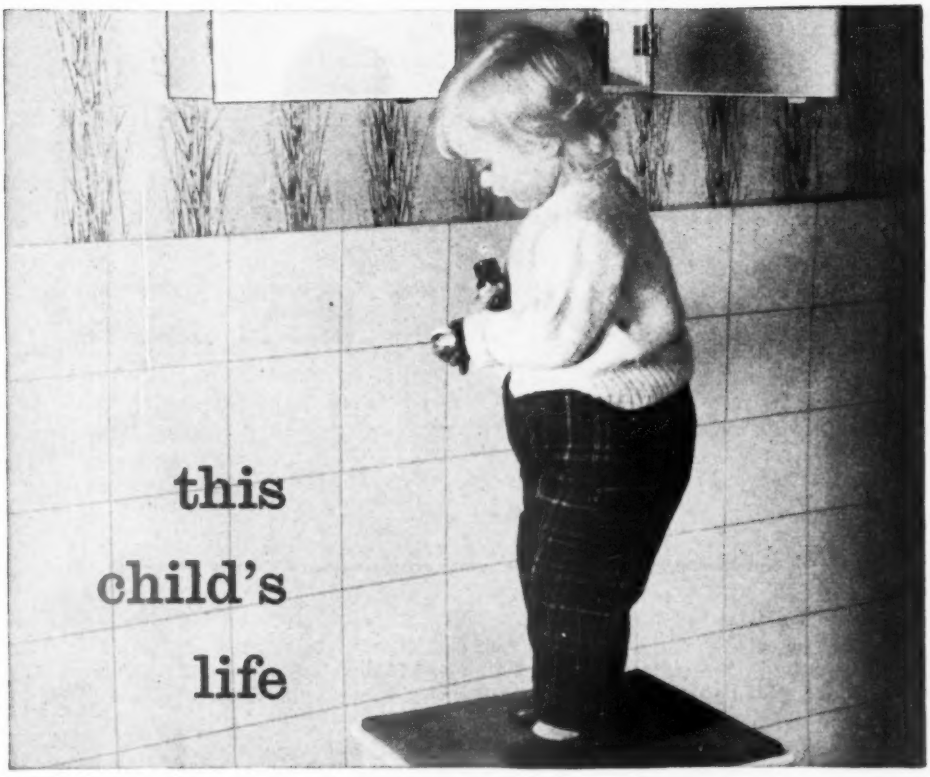

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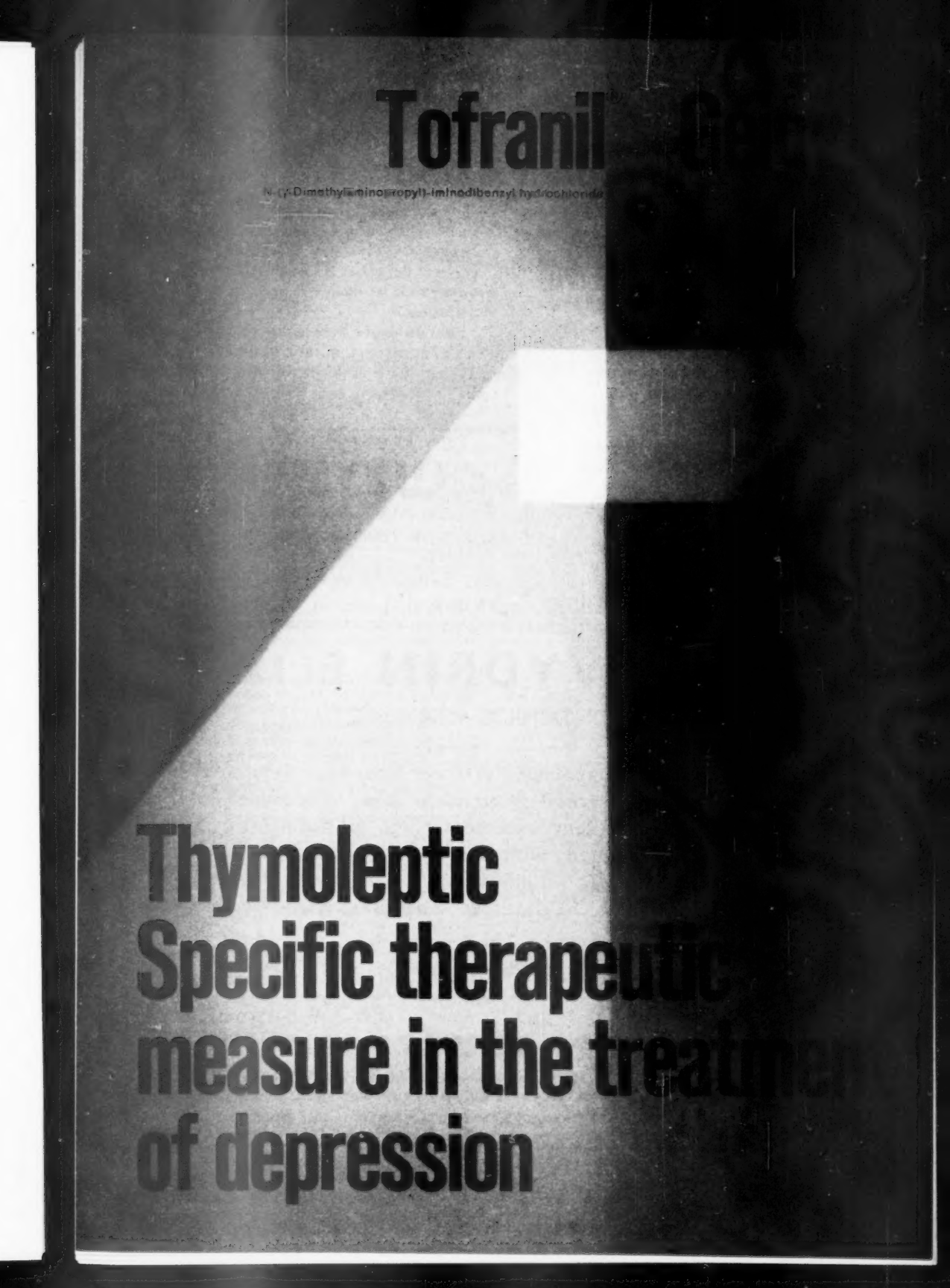
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Meeting
May 11, 1960

DISCUSSION ON THE MEDICAL MANAGEMENT AND INDICATIONS FOR SURGERY IN DIVERTICULOSIS AND DIVERTICULITIS

The Discussion was opened by **Dr. E. R. Cullinan** (*London*)

Mr. Tom Rowntree (Southampton):

Diverticulitis as Surgical Emergencies

I shall confine my remarks to the manifestations of diverticulosis and diverticulitis as they present as acute surgical emergencies; I will not discuss the cases seen as out-patients. One of the disadvantages of working in Southampton has been, until mid-1958, the lack of an efficient register of diseases, so I will give statistics for only one year—namely 1959. I have traced many cases seen before then, but the statistics would be unreliable. We serve a population of about 300,000 souls. I receive one-quarter of all general surgical emergencies over the age of 12, and in a year I deal with 520 emergencies. In 1959 there were 21 cases of diverticulitis admitted as emergencies, making an incidence of about 4%. Maclaren (1957) quoted an incidence of 10% in Edinburgh, but his total did not include all kinds of general surgical emergencies. It is unlikely that the incidence in Southampton would differ materially from that in other parts of this country. There is, however, a geographical variation in incidence of this disease. Thanks to my present registrar, Dr. B. Georgoulis from Athens, I have learned that only 5 cases of diverticulitis have been operated on in the University Hospital there in the last ten years (Georgiadis, 1960); one wonders if this discrepancy is due to environment or heredity.

In addition to the 21 cases mentioned for 1959, I have traced 20 others seen since 1953, making a total of 41 examples of acute diverticulitis. There were 24 women and 17 men, the ages ranging from 42 to 84. The majority were admitted in their first attack, with some exceptions.

Hæmorrhage.—There were 5 cases of severe hæmorrhage, 2 requiring transfusion. Brisk rectal bleeding presents a difficult diagnostic problem, and I cannot be certain that the blood came from a diverticulum. In 4, the diagnosis was made after a barium enema had revealed diverticulosis and investigation had failed to reveal any other source or cause of bleeding. One man returned a second time two years later with a recurrence of the bleeding. His films showed extensive diverticulosis. One woman, aged 47, had a normal barium enema. At laparotomy, the only operation performed in the hæmorrhage group, a solitary sigmoid diverticulum was found with a clot in it. In all cases the bleeding had ceased by the time the patient was admitted, and I agree with most other authors that operation is not necessary.

Simple inflammation.—18 cases of simple diverticulitis were seen. Abdominal pain with localized tenderness was a constant finding. In 16 the diagnosis was made clinically with subsequent radiological confirmation. Only one was admitted a second time, otherwise there had been no previous attacks, although a few had noticed some change in bowel habits. In the patients with tenderness in the left iliac fossa and in the absence of any evidence of peritoneal involvement, the diagnosis was not doubted. Treatment consisting of a short period of bed-rest and observation was always followed by uneventful recovery.

There was here no constant clinical finding other than tenderness, but in the majority the site of onset of pain was in the mid-line well below the umbilicus, shifting later to the site where tenderness was subsequently elicited. The onset-pain was therefore below the usual site where the first pain of appendicitis is experienced. I submit that, just as appendicitis presents with mid-gut pain, so diverticulitis presents with hind-gut pain, due I suggest to distension of the diverticulum, or to spasm of the sigmoid. It is only later that the pain is localized by irritation of the parietal peritoneum, and the site of localization of pain depends, as in appendicitis, upon which part of parietal peritoneum is involved. Where the diagnosis is doubtful the onset of suprapubic pain is helpful in differentiating from appendicitis.

There were two mistaken diagnoses. The first patient had maximal tenderness in the right iliac fossa, and was suspected of appendicitis. Operation revealed uncomplicated diverticulitis. Nothing was done and he had an uneventful recovery. The second misdiagnosis was in a patient with pain in the suprapubic area without any disturbance of gastro-intestinal function. She had a rounded tender mass in the pouch of Douglas without fever; torsion of an ovarian cyst was suspected. At operation diverticulitis of the

sigmoid was found. The lesion was readily mobilized, and one-stage emergency resection performed. Recovery was uneventful. She is my only example of a one-stage emergency resection for acute diverticulitis, a method advocated by Ryan (1958).

Peritonitis.—There were 11 patients with peritonitis, including one man of 42 who was admitted moribund and died within the hour; post-mortem revealed general peritonitis from rupture of a pericolic abscess. The remaining 10 underwent operation, at which the diagnosis was either confirmed or, more often, made. Only 2 had free perforation with an obvious direct communication with the lumen of the bowel. The first, a frail man of 81, was sent in as acute retention of urine (really suppression). All we could say pre-operatively was that there was general peritonitis with free gas. He made a stormy but successful convalescence following colostomy, but his general condition has precluded further surgery. The second free perforation had a previous ulcer history, and he was aged only 52. His board-like rigidity and absence of liver dullness made us suspect that he had a perforated ulcer. His pain started in the suprapubic area, and that should have indicated the correct diagnosis. At laparotomy fæces were extruding from a perforated diverticulum; the lesion was oversewn and no colostomy was made. Surprisingly he had an uneventful recovery.

The remaining 8 patients had general or pelvic peritonitis from rupture of inflamed diverticulum, without evident communication with the bowel. In only one was a confident diagnosis made before operation, but he made the diagnosis for us. In 1938, when 55, he had undergone colostomy for "inoperable carcinoma" of the sigmoid. Nine years later he was well enough for the colostomy to be closed. In 1950, he suffered perforation of a diverticulum treated by drainage only. In 1954 he had his third perforation, when I first saw him, and, not surprisingly, we made the correct diagnosis. Colostomy followed by resection I hoped would cure him, but in the following year he was again admitted—this time for small-gut obstruction from adhesions. He has been well since.

In the other 7 cases the presence of generalized rigidity with rebound tenderness determined the need for operation. In 5 the pain started below the umbilicus. Diverticulitis was suspected in these, but doubt remained until the laparotomy. In 3 there was an associated increased frequency of micturition.

The operative findings were the same in all 7, namely an inflamed diverticulum with free pus in the pelvis and turbid fluid in the rest of the peritoneal cavity. All but one were treated with colostomy, and all recovered. In no case was it possible to exteriorize the lesion, and perform a one-stage resection. One colostomy closed spontaneously soon after it had been made. 4 cases with colostomy have undergone successful resection; one is too recent yet. The one case treated with drainage alone developed a fæcal fistula, which has now healed.

The necessity for colostomy may be questioned. I think it is unwise to undertake resection in the presence of acute infection, with pus. The formation of a fæcal fistula is a nuisance; on the other hand, having made a colostomy one is committed to subsequent resection. I have been impressed by the appearance of the bowel when resection is undertaken. My cases have shown the type of thickening shown in Fig. 1, and the presence of such a lesion must threaten further trouble. Moreover in one patient, whose resection had been delayed for two years for social reasons, there was still pus in the pelvis.

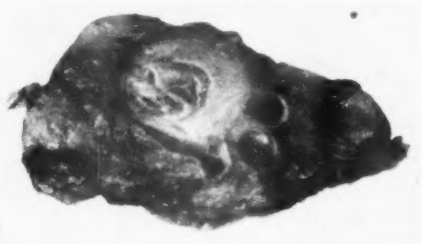

FIG. 1.—Transverse section of specimen removed three months after colostomy for acute diverticulitis.

Obstruction.—No example of acute obstruction of the colon by diverticulitis has been seen, but one patient presented with acute small-gut obstruction from adhesions.[1] She was successfully treated by separation of the adherence, the original lesion being ignored.

Pelvic mass.—4 patients were admitted with abdominal pain and a big pelvic mass, each being diagnosed as carcinoma. 3 were treated by staged resection, and 1 by one-stage resection, but they were not strictly emergencies.

Miscellaneous.—There remain 2 patients who had pericolic abscesses. One was admitted as an emergency to the medical wards with diarrhœa, thought to be dysentery. She suffered a hectic fever which failed to respond to medical treatment, although it was realized that she had an inflammatory mass in the pelvis. She started to go downhill, so I undertook laparatomy and removed surprisingly easily a large pericolic abscess. The other patient, aged 52, was admitted as a case

[1]Since this paper was read, one case of acute large-gut obstruction has been seen and treated by cæcostomy followed by resection.

of acute prostatitis. The illness had started with "influenza" followed a week later by a subumbilical pain associated with dysuria and strangury. The suspected prostatic tenderness was in fact a mass immediately above the prostate, in what turned out to be an abnormally deep rectovesical pouch. The clear urine exonerated the urinary system as the source of his trouble. The pelvic mass remained unchanged for four weeks, so I undertook laparotomy without a preoperative diagnosis. It turned out to be a pericolic abscess from diverticulitis.

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Professor John Bruce (Edinburgh):

Diverticulosis and Chronic Diverticulitis

Infection—or inflammation—is generally regarded as the most important sequel to diverticulum formation in the large bowel, and especially in the sigmoid part of the colon. The "tempo" of the so-called inflammatory process varies considerably, however, and it is difficult to separate a stage or a type that may appropriately be termed chronic. There is no doubt that acute diverticulitis occurs, with fever, pain, guarding and tenderness in the left iliac fossa and a tendency to go on to pericolic abscess formation; but recurrent non-febrile episodes of left iliac pain, with only tenderness and thickening in the line of the pelvic colon, are more difficult to interpret, and in the not infrequent absence at eventual operation in such cases of signs of present or former inflammation the mechanism of symptoms is by no means always clear. In fact there have been few comprehensive studies of the pathology and the course of diverticular disease, and as a corollary to our relative ignorance of its natural history, there is lack of definition in our therapeutic approach. As a first consideration, therefore, it is wise to assess the clinical significance of uncomplicated colonic *diverticulosis*.

Diverticulosis

Diverticulosis is unquestionably a common deformity of the colon. Its frequency has been reported by many observers but the findings of Ochsner and Bargen (1935) are as reliable as any, and those workers found diverticula in 6–7% of autopsies. The incidence in routine barium enemas is 8·5% (Pemberton *et al.*, 1947). On the basis of these figures, there are presumably about four million victims in the United Kingdom, of whom, fortunately, only a small number require surgical treatment.

The diverticula are almost invariably multiple, though rarely a solitary diverticulum may form in the cæcum or in the cæcocolic tract. No part of the colon is immune, but the pelvic colon is generally most involved, and diverticulitis is therefore more common in this segment. The evidence of repeated opaque enemata suggests that diverticulosis, though usually localized to begin with, may progressively involve more and more of the colon until the whole is affected.

The view is widely held that, in the absence of inflammation, colon diverticula have no clinical significance. This is not the case, because the experience of most of us includes examples of sudden perforation, or of severe hæmorrhage without a preceding stage of diverticulitis. Nevertheless, the majority of persons with diverticulosis have no symptoms, or at most some "irritability" of the bowel; but even in those with clinical effects sufficient to prompt a diagnostic barium enema, diverticulosis for the most part remains uncomplicated pathologically. Boles and Jordan (1958) have put a numerical value on the likelihood of later sequelæ. In an eleven to twenty-seven year follow-up study of 294 patients with mild abdominal symptoms and radiological diverticulosis, 60% had no further trouble. Of the remainder, 25% developed "diverticulitis" on one or more occasions; hæmorrhage, obstruction with fistula formation and perforation each occurred in 5%. It is worthy of note that in more than half the bleeders, a quarter of the obstructions and a third of the perforations there was no preceding clinical diverticulitis, while of those who developed diverticulitis less than half came to operation. Simply stated, the observations of Boles and Jordan suggest that only 10% of patients who start off with *symptomatic* diverticulosis "go wrong", and may need surgery.

Subacute and Chronic Diverticulitis

Like the acute manifestations of diverticulitis, the subacute and chronic forms, for all practical purposes, are confined to the pelvic and descending colon. Clinically they present in a variety of ways: (1) Following the resolution of one or more attacks of acute diverticulitis the pelvic colon remains thickened and tender; there is a change in bowel habit, pain in the left iliac fossa, often a raised erythrocyte sedimentation rate and some upset in health. (2) Following the subsidence of acute infection a chronic pericolic abscess may develop in the left iliac fossa. (3) Without a preceding frank acute diverticulitis an indolent pericolic abscess may form in the left iliac fossa. (4) There may be a history of recurring attacks of fever, left iliac pain and malaise not severe enough to justify a label of acute diverticulitis. (5) There may be a more or less constant left iliac fossa pain with exacerbations, accompanied by change in bowel habit but without fever.

Apart from the inherent importance of these clinical types as causes of discomfort, ill-health and disablement, each is important as the potential prelude to more serious complications, especially obstruction and fistula formation. For this reason a more aggressive attitude is increasing; and the evidence of Boles and Jordan (1958) that the incidence of complications rises with the number of attacks of diverticulitis to nearly 60% provides statistical support for such a policy.

In practice, however, there is still a proper unwillingness to embark on radical colon surgery, in the absence of obvious and severe local pathological signs or a well-founded clinical conviction that if left alone more difficult and dangerous complications are all but inevitable. Retrospective assessment of the chronic cases that have come under my observation clearly establishes that more than one indication was present before operation was advised and that the need for operation was declared by the onset of complications or by uncertainty about the diagnosis.

Despite the comparative safety of modern colon surgery, a cautious policy is certainly wise, because the majority of patients are elderly, and many are in the "poor risk" category on account of chronic bronchitis and obesity. Furthermore, there is often accompanying but unrelated disease elsewhere in the abdomen. Thus some 6% of patients with diverticulitis have gallstones and a hiatus hernia—Saint's triad; and many are the victims of peptic ulceration.

When surgery is decided upon, the ideal operation is a one-stage resection with end-to-end anastomosis. This may be inadvisable in elderly, obese or otherwise unfit patients, in whom a transverse colostomy is safer and wiser; or primary resection may be unduly hazardous when there is a pericolic abscess or an adherent pericolic granulomatous mass, when a colostomy is indicated. Usually—though not invariably—the symptoms of diverticulitis disappear after colostomy, which should be regarded as a prelude to resection later, though some patients become so well conditioned to it that further surgery is refused. In this event, there is no need to press the issue if the diagnosis was not in doubt, especially in those up in years. It is unwise to close the colostomy without resection even after a considerable symptom-free interval, for the affected part of the colon usually contracts, and recurrence of symptoms is almost invariable.

The interval between colostomy drainage and excision is conventionally about four to six months. Properly it should depend on assessment of the factors determining the colostomy, and the local pathology, the longer interval being necessary when there is a large adherent inflammatory mass; otherwise, a few weeks suffice for the shrinkage of distended colon proximal to the "lesion" and for the resolution of most degrees of diverticulitis.

The amount of bowel to be removed is usually easy to decide; the operation is for "diverticulitis"—whatever that implies—and no attempt should be made to excise all the diverticula-bearing colon. The distal level of section is through the lowest part of the pelvic colon, the proximal at a convenient point immediately above the diseased segment, though care should be taken not to include an uninflamed diverticulum in the suture line; the wall of a diverticulum is thin and if a suture penetrates it, leakage is almost certain. In practice, removal of 12–14 cm of pelvic and descending colon usually suffices, but in order to restore continuity without tension it is generally wise to mobilize the descending colon and the splenic flexure. Resection for diverticulitis is not only less extensive but less radical than for carcinoma. It is unnecessary to ligate the inferior mesenteric artery or its main branches, or to resect mesentery; but it is usually wise to visualize the left ureter and to ensure its preservation.

Whether or not a temporary colostomy should be made after resection is a matter for individual judgment, bearing in mind that resections for diverticulitis are followed by infective intraperitoneal complications sufficiently often to be disturbing. In the obese, it is easy to perforate an unsuspected diverticulum with a suture; and in the elderly the vessels are often sclerotic, and the marginal anastomosis less adequate. In both events, post-operative gaseous distension may precipitate a leak. Furthermore, in many cases the fixation of the diverticulitic colon is marked, and satisfactory mobilization may demand the opening up of inflamed tissue planes. A temporary colostomy may be a small price to pay for safety.

Rectal Bleeding

That rectal bleeding is frequently associated with diverticulosis and diverticulitis is not disputed. Thus in Edinburgh Royal Infirmary it was an obvious feature in 10% of 112 cases admitted to the surgical division with a diagnosis of diverticulitis: and Rushford (1956) in a survey of 6,000 cases in the literature assessed the incidence of bleeding as 17%. In smaller series, Lloyd-Davies (1953), Mobley *et al.* (1957) and Keith and Rini (1957) recorded its occurrence in 18·5%, 7·4% and 19% respectively. Though the association is admitted, the significance of the bleeding is disputed, and Gilchrist and Economou (1955) and De Cosse and Amendola (1957) consider that it is never, or only rarely,

due to the diverticulitis, but most commonly to coincidental polyps or carcinoma. My experience leaves me in no doubt that bleeding may occur from granulations or from ulceration secondary to diverticulitis, and from ulceration at the mouth of even an uninflamed diverticulum. The occurrence of bleeding is favoured by the distribution of the vessels related to the diverticula. Noer (1953) by radiology after opaque injection showed that there is a vascular circle around the neck of each sac, and erosion by a fæcolith is a distinct possibility.

The hæmorrhage may be massive and sometimes exsanguinating; this catastrophic type occurs almost always in elderly (and presumably arteriosclerotic) subjects. In 6 such patients whom I have encountered, preceding bowel symptoms were absent or minimal, but diverticulosis was extensive. All were managed conservatively, and fortunately recovered, though in 2 there was recurrence of bleeding at intervals of four years and six months respectively.

Reports of surgical intervention in massive hæmorrhage are few, and fortunately the necessity rarely arises. It seems to be difficult to pin-point the site of hæmorrhage at operation, but if there is an obvious segment of diverticulitis it seems reasonable to resect this and trust that the source of the bleeding has been removed. This has not always been effective in controlling the bleeding and a patently abnormal length of colon is not invariably present. Under these circumstances, it may be wise to carry out an extensive—or even complete—colectomy with ileo-rectal anastomosis. The situation, in fact, is similar to that obtaining at operation for hæmatemesis at which no obvious cause is found.

Moderate or minor bleeding is of more importance than massive hæmorrhage on account of its greater frequency and of the diagnostic problem it poses. It may be episodic, persistent, related or unrelated to defæcation, and occur with or without other bowel symptoms. Neither a known previous diverticulitis, a history of diverticulitis nor the radiological demonstration of diverticula justify the assumption that bleeding is related to the disease, for cancer and diverticulitis occur together in 12% of patients; and adenomatous polyps are also common, while piles or an anal fissure can give rise to brisk hæmorrhage. Proctoscopic and sigmoidoscopic inspection are imperative, and scrupulous skilled radiological examination. The presence of a lump on abdominal examination, bleeding from above the limit of the sigmoidoscope, and an equivocal radiological report are indications for operation; so too is persistence of bleeding despite conservative treatment of the diverticulitis.

Obstruction

Secondary fibrosis with stenosis—first recognized by Graser (1898)—is the commonest and most important complication of diverticulitis. The stenosis may be localized, or a longish segment may be involved; and as a rule the pelvic colon or lower descending colon is implicated.

It is rare for operation to be undertaken for diverticulitis until an obstructive element is recognized in the symptomatology, but when we refer to obstructive diverticulitis we have in mind those patients whose presenting or principal manifestation is serious interference with the passage of intestinal contents.

When obstruction is chronic, the difference between diverticulitis and carcinoma may tax the resources of the clinician and the radiologist before operation, and of the surgeon at operation; and in any event the two conditions frequently co-exist. The diagnostic problem is accentuated when there is also rectal bleeding for which no rectal cause is apparent, or when there is a palpable swelling in the iliac fossa. A protracted history of bowel trouble, a more frequent history of colicky pain, more pronounced tenderness in the iliac fossa, and the occurrence of *massive* hæmorrhage no more than favour a diagnosis of chronic diverticulitis, and we are forced to rely largely on the radiological examination in making the differential diagnosis. Unfortunately, the picture is equivocal in a considerable number of cases; even the length of the diseased segment, or the other criteria of benignity—preservation of mucosal pattern, ill definition of the margins of the filling defect—may be no more than suggestive of diverticulitis.

The obvious course in such circumstances—if not in all forms of chronic obstructive diverticulitis—is operative exploration. Even here it may be impossible to distinguish between an inflammatory lesion and cancer. If the local conditions permit a resection of the lesion, the operative procedure for carcinoma is quite different from that required for diverticulitis: and if in the presence of an adherent mass it is elected to make a proximal colostomy, the interval allowed to elapse before subsequent resection must be dictated by our ability or otherwise to exclude carcinoma. If this is possible, an interval of some months may be allowed for the subsidence of the peridiverticular inflammatory reaction; otherwise there is no justification for postponing resection for more than a few weeks.

Fistula Formation

Fistulæ into neighbouring structures may follow perforation either of an inflamed adherent diverticulum or of a pericolic abscess, more

commonly the latter. In the first case, there may be little or no pericolic inflammatory reaction; in the other, the structures are incorporated in an inflammatory mass. The most frequent and most important lesion is the colo-vesical fistula, and next in frequency the colo-vaginal variety.

Colo-vesical fistula.—Diverticulitis is the commonest cause of fistula between the bladder and the colon; carcinoma of the sigmoid or of the bladder is a rarer precursor, and other forms are unusual. It is predominantly a male complication, the intervention of the uterus sparing the female this distressing sequel.

Clinically the important feature of colo-vesical fistula secondary to diverticulitis is the high incidence of preceding urinary symptoms, varying from urgency and frequency to complete retention. These evidences of impending fistula may continue for weeks or months; or there may be recurring episodes; and they should be regarded as a strong indication for operation.

In the majority, the establishment of a fistulous communication is followed initially by an intense and diffuse cystitis, and fæces and gas are passed in the urine. Later the cystitis may partially subside, leaving a subacute or chronic inflammation to which some patients acquire a remarkable degree of tolerance. In a few, symptoms become minimal and the fistula appears to be compatible with reasonable health.

The classical case presenting with pneumaturia and cystitis offers no particular diagnostic difficulty. Cystoscopically there is diffuse cystitis and often extreme œdema in the neighbourhood of the fistula, though in more than half the cases a fistulous opening is not identified. Though it should always be done, sigmoidoscopic examination is rarely helpful, for fixation of the colon makes the procedure difficult and it is unusual to see the openings of the diverticular sacs. Lack of mobility of the sigmoid, narrowing of its lumen, œdema of the mucosa and angulation of the bowel are suggestive, and when the causal lesion is doubtful it is sometimes possible to demonstrate that a carcinoma is present. Radiological studies may demonstrate the presence of diverticulitis unequivocally; unfortunately, however, fistula formation in diverticulitis is often a sequel to the onset of obstruction and the radiologist may not be able to exclude carcinoma with confidence.

When the fistula has become chronic there may be difficulty in establishing the diagnosis. The bladder mucosa may look normal, though there is commonly œdema or some granulations at the site of the communication. Careful microscopic examination of the centrifuged urine may reveal fæcal debris, and culture of the urine may yield intestinal organisms. The introduction of methylene blue into the bladder and its recognition in the fæces at sigmoidoscopic examination may also offer confirmatory evidence.

The treatment of colo-vesical fistula is surgical, and nothing short of resection of the diseased segment of colon can guarantee a cure. Attempts to separate the viscera and close the apertures are not worth considering, even after a preliminary colostomy.

The safest programme is a defunctioning transverse colostomy followed after four to six weeks by excision of the diseased segment and sound closure of the bladder opening after excision of its sclerosed margin. A more aggressive approach is sometimes both possible and justifiable —as, for example, when there is no pericolic abscess and only minimal inflammatory adhesions and when the fistula is at or near the dome of the bladder. Here primary resection is no more difficult than in other forms of diverticulitis; and the justification for it is the not infrequent failure of a preliminary colostomy to control the bladder infection. This is particularly apt to occur when there is a urinary obstruction from prostatic enlargement or urethral stricture, persistence of the abscess cavity, or a second fistula between the colon and the ileum—an uncommon association.

In fat patients and in those with a low fistula or an intermediate abscess between colon and bladder a preliminary colostomy is indicated. The position is probably best summed up by saying that a two-stage operation carries a slightly greater margin of safety and allows cleansing of the bowel before excision is attempted. Furthermore, if the interval between colostomy and resection is kept to a minimum the prognosis, even if the lesion should prove to be malignant, is not greatly worsened. Nevertheless, it is often possible to resect the colon and repair the fistula at a single sitting. The use of the method demands sound and cautious judgment.

Colo-vaginal fistula.—The passage of fæces and gas through the vagina is almost as distressing as fistula-formation into the bladder. Colo-vaginal fistula following diverticulitis is usually between the lower part of the pelvic colon and the upper posterior wall of the vagina, but the diseased colon often flops over to become adherent to the rectum. In consequence there is often considerable perirectal inflammation, which contraindicates attempts at single-stage cure. Resection of the diseased colon and closure of the vaginal opening should invariably be preceded by a defunctioning transverse colostomy.

Cutaneous fistulæ and sinuses. — The spontaneous rupture of a pericolic abscess on the

abdominal wall or an operation for the drainage of an abscess may leave a chronically discharging sinus in the left iliac fossa. This is often of little moment. The discharge may be fæcal, mucoid, or purulent but is small in amount. Spontaneous closure is the rule but persistence may demand resection of the diseased colon after suitable bowel preparation.

Sometimes a pericolic abscess becomes adherent to the pelvic floor and ruptures through it into the ischiorectal fossa. Spontaneous rupture on the perineum or operative drainage on a supposed ischiorectal abscess may then leave a high level anorectal sinus or fistula which does not heal until the affected part of the colon has been excised and the infected ischiorectal fat is removed along with the opening in the pelvic floor. These measures should always be preceded by a defunctioning colostomy.

In conclusion, the indications for operation in chronic diverticulitis are: (1) Frequent and disabling attacks of left iliac fossa pain, (2) the development and persistence of urinary symptoms, (3) the onset of symptoms of obstruction, (4) occasionally, bleeding, (5) fistula formation, and especially (6) inability to exclude cancer.

The operation of choice is primary resection of the affected colon. Preliminary colostomy should be established when primary resection is dangerous because of the general condition, age, or obesity, or because of the severity of the local pathology. Resection should invariably follow colostomy, and a shorter time interval between the two procedures than the orthodox four to six months is desirable.

Simultaneous temporary colostomy is indicated in fat subjects, when there is any suspicion of the adequacy of the marginal vessels, when there is any tension on the anastomosis and when mobilization of the bowel has led to extensive opening up of tissue planes.

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Mr. Ronald W. Raven (London):

The differentiation of diverticulosis from diverticulitis influences the treatment of these conditions.

Diverticulosis is present in about 5% of all persons over 40 and 10 to 20% of them develop diverticulitis. Those who are obese or habitually constipated are more likely to suffer the inflammatory complication. Uncomplicated diverticulosis is often asymptomatic but slight or profuse rectal hæmorrhage sometimes occurs. Sigmoidoscopy may reveal the site of the bleeding in the sigmoid colon and sometimes blood is seen coming from a diverticulum. An associated polyp or carcinoma may be the cause of the hæmorrhage (Fig. 1). In cases with hæmorrhage a partial colectomy may be necessary.

FIG. 1.—Diverticulosis of sigmoid colon with an associated polyp which caused rectal hæmorrhage and required partial colectomy.

Diverticulitis is a serious, disabling, progressive disease which often necessitates frequent and prolonged admissions to hospital. The irreversible changes in the colon cause constant and severe suffering and at any time a lethal complication may develop. The sigmoid segment of the colon is commonly affected. Until fairly recently surgical treatment was reserved for those with complications and many palliative operations were done. When curative operations were performed they were carried out in stages dictated by the pathological changes in the colon. This practice is untenable now and is superseded in the early phase of diverticulitis by a one-stage operation designed to restore the patient to normal health.

My remarks are based on a study of the cases of diverticulitis seen at the Gordon Hospital during 1947 to 1958, comprising 425 patients; 190 (44·7%) were males, and 235 (55·3%) were females.

Indications for Surgical Treatment

During recent years the indications for surgical treatment have broadened and many more patients are undergoing operation in an earlier stage of the disease. The number of patients operated on in this series are shown in Table I.

Table I.—The Gordon Hospital. Diverticulitis
Number of Operations 1947 to 1958

Sex	No. operated	No. of deaths
Males	45 (23·7%)	0
Females	36 (15·3%)	1
Total	81 (19%)	1 (1·2%)

The patients for whom surgery is required are divided into two groups.

(1) *Patients with complicated diverticulitis.*—This includes patients with internal and external fistulæ; partial or complete intestinal occlusion; perforation causing a pericolic abscess or acute diffuse peritonitis; an associated polyp which may obstruct a stricture or cause hæmorrhage; an associated carcinoma.

(2) *Patients with uncomplicated diverticulitis.*—This includes patients with recurrent attacks of diverticulitis uncontrolled by medical treatment; patients under 50; patients with persistent deformity of the sigmoid in the barium enema; patients with rectal hæmorrhage when other causes of bleeding are excluded; patients with urinary symptoms; patients with diverticulitis in whom carcinoma cannot be excluded; patients who live in remote places where a complication might be disastrous.

Certain points are worthy of stress in this group.

Recurrent attacks.—A number of patients remain undiagnosed for variable periods because the clinical picture of diverticulitis is often atypical. It varies from person to person and from episode to episode. In this series the following were the symptoms in order of frequency: abdominal pain; diarrhœa; constipation; rectal hæmorrhage; flatulence. Sigmoidoscopy is often more difficult when diverticulitis is present, mobility of the sigmoid is limited and one or more diverticula may be seen.

In the past these patients were treated medically for it was the practice to operate only when a complication occurred. Many suffered considerably from their symptoms and some went to different hospitals in search of relief. The following is a typical case:

Case I.—Female, aged 67, admitted to hospital with abdominal pain.

History.—Many years abdominal pain of an aching character, sometimes severe, associated with nausea and vomiting. She had been investigated in two hospitals for cholecystitis and peptic ulceration with negative results. During the last two years she has required a laxative.

On examination.—Thin. Abdomen distended and tympanitic in the lower half; tenderness in left lower quadrant. Rectal examination negative. Barium enema: The colon filled freely with diverticulitis of the sigmoid colon; a few diverticula are present in the transverse colon. Immediate evacuation was good.

Operation.—Partial colectomy with end-to-end anastomosis. *Specimen:* Diverticula are present throughout the specimen in three longitudinal rows. Some thickening of the bowel suggesting old chronic inflammation.

Result.—Uninterrupted recovery.

Patients with persistent deformity of the sigmoid in barium enema radiographs.—When considering the treatment the radiological appearances of the colon are noted as well as the symptoms. If the radiographs show distortion of the colon and associated spasm this means that permanent and progressive changes are present and surgical treatment is necessary.

Patients under the age of 50.—Diverticulitis is a progressive disease whose effects often increase in severity with advancing age. Many patients develop complications later when they are less able to bear them and others suffer abdominal pain and other symptoms for years, and eventually require surgical treatment in old age. These effects are prevented by certain operations and this is advisable for patients with diverticulitis under 50. The following patient had severe diverticulitis for years, requiring surgery late in life.

Case II.—Female, aged 82, admitted with severe abdominal pain.

History.—Many years' pain in the left side of the abdomen. Three years ago she began to have vomiting and diarrhœa; rectal hæmorrhage necessitated the transfusion of 2 pints of blood. She had been in three different hospitals but the lower abdominal colic had persisted; for the last three weeks she was given pethidine to control it. She is constipated and requires an aperient.

Past history.—Hæmorrhoidectomy 1911; appendicectomy 1914; cholecystectomy 1937.

On examination.—General condition satisfactory. Scars of previous operations sound; no abdominal distension or visible peristalsis. Tender, palpable pelvic colon. Edge of the liver palpable. Rectal examination negative.

Investigations.—Barium enema: Marked diverticulitis of lower descending and sigmoid segments. Diverticula present in ascending and transverse parts of colon. Hb 97%. Liver function tests normal.

Treatment.—Conservative treatment was tried without relief.

Operation (19.1.60).—Left hemicolectomy; there were dense adhesions around the pelvic colon.

Specimen.—Numerous diverticula, most marked at the distal end of the colon. There is an area of diverticulitis 8 cm long in the sigmoid colon with the lumen considerably narrowed and much thickening and inflammation of diverticula. Histology showed diverticulitis.

Result.—Uninterrupted recovery.

Patients with rectal hæmorrhage.—This is recognized as a common symptom of diverticulitis, with an incidence of 10 to 30%. Rectal hæmorrhage was the fourth common symptom in this series. The bleeding may be slight and remittent, but it can be severe and persistent and even exsanguinating. For the last an emergency partial colectomy is necessary. Rectal bleeding may be the presenting symptom of diverticulitis and can overshadow the other symptoms. The mucous membrane of the sigmoid and rectum may be red and granular and bleeds easily. Sometimes the hæmorrhage is caused by an associated polyp or carcinoma. The following is the history of a patient with diverticulitis who had recurrent rectal hæmorrhage for several years and whilst in hospital had severe bleeding.

Case III.—Female, aged 63, admitted with persistent diarrhœa for two and a half years.

History.—Mucus and blood occasionally passed *per rectum.* In 1957 a barium enema showed diverticulitis of the descending colon. This was treated conservatively. In July 1959 the X-ray showed diverticulitis of the descending and sigmoid colon. She was treated with hydrocortisone and cortisone. Seven weeks ago she had diarrhœa every two hours with vomiting. The abdomen became distended and bed-rest was necessary.

On examination.—Patient looked ill. Marked tenderness and thickening in the region of the pelvic colon. Rectal examination negative.

Investigations.—Hb 71%. Barium enema: Colon filled freely; diverticulitis of the sigmoid colon with marked spasm. Sigmoidoscopy: The mucous membrane of the upper part of the rectum was granular and bleeding. The patient was treated conservatively but a pericolic abscess developed.

Operation (6.10.59).—Exploratory laparotomy and transverse colostomy. A large inflammatory swelling involved the sigmoid colon. In the immediate post-operative period severe rectal hæmorrhage occurred. On 12.10.59 the Hb was 49% and 8 pints of blood were given. Her condition improved and after convalescence she was readmitted.

Operation (29.12.59).—Partial colectomy with end-to-end anastomosis. Specimen: 15 cm of colon which is thickened with diverticula penetrating the muscle coat and narrowing of the lumen. Microscopy: diverticulitis with active inflammation.

Operation (26.1.60).—Closure of transverse colostomy.

Result.—Uninterrupted recovery.

Patients with urinary symptoms.—These patients have symptoms of cystitis, including frequency of micturition, dysuria and hæmaturia, due to the adherence of the inflammatory sigmoid swelling to the wall of the bladder; an abscess may form between the two. Subsequently a vesicocolic fistula develops. Surgical treatment is necessary in diverticulitis as soon as urinary symptoms are experienced, for a vesicocolic fistula might be prevented. The following case history is illustrative.

Case IV.—Male, aged 50, admitted with abdominal pain.

History.—Four attacks of abdominal pain thirteen, five, two years and one year ago. The pain starts in the left iliac fossa and gradually worsens over three days. Diarrhœa occurs and defæcation is painful; burning micturition with frequency. The attacks last about two weeks. He was twice admitted to another hospital; in 1957 a "slightly tender mass in the left iliac fossa and the mass was palpable on rectal examination at the tip of finger". He was readmitted in 1958 as an emergency with abdominal colic, diarrhœa, nausea and anorexia. A tender mass was palpable in the left iliac fossa on rectal examination. Chronic diverticulitis and peridiverticulitis was diagnosed and the patient was treated with antibiotics. He improved and the mass in the left iliac fossa became impalpable.

On examination.—Thin; the pelvic colon is tender and thickened. On rectal examination there is a soft tender swelling high on the left.

Investigations.—Hb 91%. Urine contained many red blood cells and pus cells; *B. coli* and *Str. fæcalis.*

Operation (27.1.59).—Partial colectomy with excision of the upper third of the rectum. There was a large inflammatory œdematous mass involving the sigmoid colon adherent to the wall of the bladder with an abscess between the two.

Specimen.—17 cm of colon. Two rows of orifices in the mucosal surface lead into diverticula. The bowel wall is thickened; there is much fat on the serosal surface and the appendices epiploicæ are adherent to one another with overlying congestion of the peritoneum. On section of the bowel transversely small abscesses are seen. Microscopy: extensive fibrosis and purulent inflammatory changes in the serosa; abscess cavities are seen and in one section inflammatory changes extend from the base of a diverticulum into the serosa.

Result.—Uninterrupted recovery.

Patients with diverticulitis and a possible carcinoma.—A carcinoma may be present in the colon affected by diverticulitis but it is generally agreed that the risk of this is no greater with diverticulitis and diverticulosis than in the normal colon. It may be impossible to decide clinically and radiologically whether these diseases co-exist in the same segment of the colon and doubt may persist on exploratory laparotomy. When an associated carcinoma is suspected a radical left hemicolectomy should be performed. The following is an illustrative case.

Case V.—Female, aged 56, admitted with increasing constipation.

History.—Four years ago she had rectal incontinence for which a reconstruction operation on the anorectal sphincters was performed. At that time a barium enema showed moderate diverticulitis of the pelvic colon and lower part of the descending colon. Immediate evacuation was limited and at twenty-four hours there was an appreciable amount of barium in

the colon. Conservative treatment was instituted. The patient was well until one year ago when she developed constipation. Sometimes the bowels are not opened for four days and small stools are passed. Occasional pain in the left iliac fossa has become more severe during the past week when fever developed. No blood or mucus was noticed in the stools. Micturition is normal.

On examination.—Obese. On abdominal examination there is a firm tender lump in the left iliac fossa. Liver not palpable. Rectal and vaginal examinations negative.

Operation (1.3.60).—Left hemicolectomy. At laparotomy, a carcinoma and diverticulosis found in the sigmoid colon.

Specimen.—62 cm of the colon; in the middle and completely encircling the bowel is a raised papilliferous tumour 4 cm long and infiltrating the muscle coats but not the pericolic fat. No other polypoid lesions seen in the colon. Above and below the tumour are numerous diverticula with wide necks. The muscle coats are greatly thickened, and the wall of the colon is thrown into numerous small folds. No mucosal ulceration besides the tumour area seen. Histology: The tumour is a well-differentiated adenocarcinoma which has just penetrated the muscle coats, and there is little invasion of the pericolic fat. The blood vessels and lymph nodes are free of tumour. One section shows several diverticula, thickening of the muscle coats, and prominent mucosal folds. No inflammatory reaction seen.

Patients who live in remote places.—As the complications of diverticulitis are common and serious it is advisable to carry out surgical treatment for those patients who live in remote places where it is difficult to find a surgeon and complications might therefore prove disastrous.

Operations for Diverticulitis

The following operations are performed for the different indications which may present.

One-stage Operations

(1) *Excision of a solitary diverticulum.*—Inflammation can occur in a solitary diverticulum when the remainder of the colon is normal. Under such circumstances excision of the diverticulum is performed with repair of the colonic wall. Where inflammation of the diverticulum has spread to the adjacent colon which is thickened and œdematous, a partial colectomy is required.

(2) *Partial colectomy* can be performed with safety when there is minimal intestinal occlusion, the affected colonic segment is short, the inflammation is chronic or mildly subacute and the bowel ends for the anastomosis are not œdematous.

(3) *Left hemicolectomy* is done when an associated carcinoma is suspected; the sigmoid and descending parts of the colon are the site of diverticulitis; œdema has spread into the descending colon; extensive diverticulosis of the descending colon is present; and when partial colectomy would result in tension at the colonic anastomosis. In the latter case the more mobile transverse colon is anastomosed with the rectum.

After a one-stage operation leakage at the anastomosis may occur about the tenth post-operative day. There is local abdominal pain, rigidity and tachycardia. A temporary transverse colostomy should be instituted at once. It is closed about three weeks later.

(4) *Total colectomy with an ileo-rectal anastomosis* is performed when diverticulitis of the sigmoid colon is associated with severe diverticulosis of the entire colon and cæcum.

Multiple Stage Operations

Two-stage operation.—When the bowel is loaded with fæces, or there is tension at the anastomosis, temporary transverse colostomy is established at the same time as the partial colectomy or left hemicolectomy.

Three-stage operation.—A temporary right transverse colostomy is instituted at the exploratory laparotomy when there is acute or severe subacute inflammation of the affected colon, partial occlusion of the lumen of the bowel with proximal fæcal retention, or œdema of the bowel wall beyond the site of resection.

After four weeks (shortened when there is a suspected carcinoma) resection of the affected colon is performed. After a further four weeks the colostomy is closed after a barium enema has confirmed that the anastomosis has healed soundly.

When a colostomy has been instituted as the only surgical treatment for diverticulitis it must not be closed unless the affected part of the colon has been excised, otherwise the diverticulitis will recur.

Some Technical Points in the Surgical Treatment.

The whole of the diseased colon must be excised to prevent recurrent diverticulitis. This entails, in the average case, excision of about 20 cm of affected colon. It is important not to overlook any diverticula in the upper end of the rectum. The latter is divided at a safe distance below the disease to prevent recurrent diverticulitis or a fistula.

The anastomosis is usually performed in two layers; an outer seromuscular layer of interrupted sutures of fine thread, and an inner layer of continuous catgut sutures through all layers of the bowel. A soft rubber drain is placed down to the anastomosis and left in position until the bowels open about the fifth post-operative day.

Acknowledgments.—I wish to thank my colleagues at the Gordon Hospital for permission to study the case records, and also Mr. C. I. Cooling, F.R.C.S., who compiled the statistical data.

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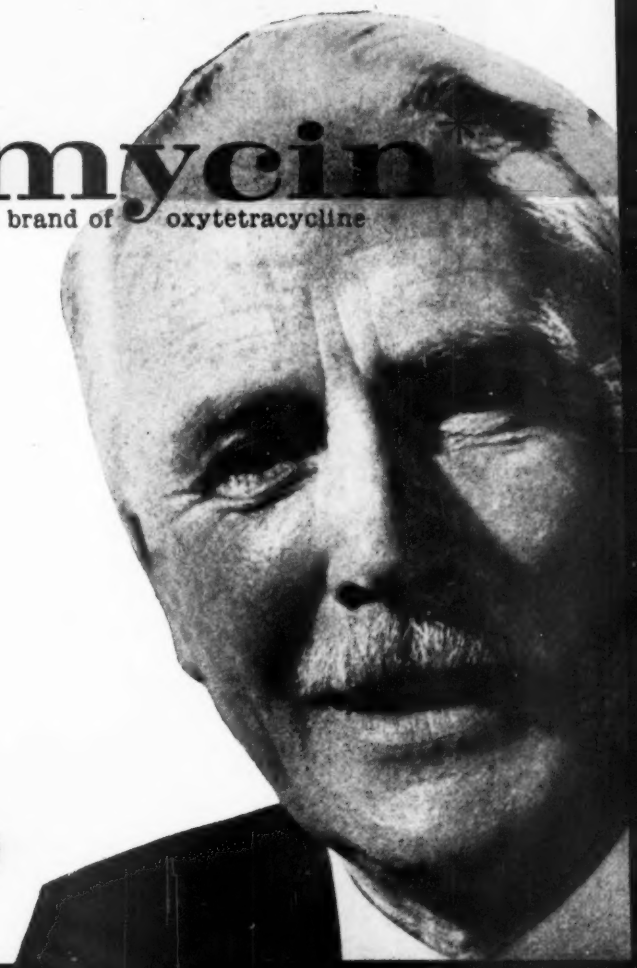

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JOINT MEETING WITH THE FOURTH INTERNATIONAL GOITRE CONFERENCE

The History of Endemic Goitre and Cretinism in the Thirteenth to Fifteenth Centuries[1] [*Abridged*]

By Professor F. MERKE, M.D.
Basle, Switzerland

THE standard histories of medicine tell us very little about endemic goitre and cretinism in the Middle Ages and I do not propose to repeat what can be read there. Instead, I shall attempt a hitherto unexplored approach to the mediæval history of goitre and cretinism.

There are four ways to investigate endemic goitre and to document its incidence in earlier centuries: (1) Medical literature; (2) study of proper names (family and place names connected with "goitre"); (3) non-medical literature (Roman classics, encyclopædias, belles-lettres, minnesingers' songs, epic poems, novels, short stories, &c., from the Middle Ages); (4) pictorial representations of goitre (manuscript illuminations, drawings, wood-cuts, paintings, sculptures).

With regard to point (1). If one traces back medical literature over the centuries, one has to admit that the trail is lost in the Middle Ages. It is not until about the year 1300 that we first encounter two rather laconic references by physicians to goitre as an endemic disease, i.e. in the works of Arnaldus de Villanova (goitres in Lucca) and Lanfrancus (goitres in Lombardy). Some hundred years later (1418), a high incidence of goitre was reported by Valescus de Taranta in the Pyrenees (Foix) and, finally, by Montagnana ("among the Germans", probably in the South Tyrol). Another century then elapsed before Paracelsus described the occurrence of goitre in Pinzgau in the neighbourhood of Salzburg (1527). Not until the eighteenth and nineteenth centuries does the documentation in medical literature dealing with endemic goitre become somewhat more plentiful.

The second possibility (2), the *study of proper names connected with goitre*, an avenue hitherto unexplored, enables us to go further back in time. This line of research is concerned with the names of families and localities associated with the word "Kropf" in German, "goitre" in English and French, "gozzo" in Italian, and "bocio" in Spanish-speaking regions. These investigations have not yet been completed, but I have already managed to trace back certain place names connected with the word "Kropf" to the twelfth century and family names to the eleventh century.

As to point (3), the only *non-medical literature* hitherto drawn upon in medical history has been the writings of the Roman authors Vitruvius, Pliny the Elder, Juvenal and Ulpian, who make only brief and vague references to goitre as an endemic disease in Alpine districts. But the non-medical literature of the Middle Ages has so far never been exploited as documentary evidence of endemic goitre, although it affords a surprising wealth of information in an epoch when medical literature still had nothing to offer. Space does not permit the discussion of details here, but we shall revert later to the encyclopædias of the thirteenth centry, in connexion with our fourth and last avenue of approach.

(4). A study of the incidence and role of *goitre in pictorial art*, including illuminated manuscripts, is yet another approach which has so far been scarcely explored. It provides an interesting insight into the role of goitre in the history of art and civilization. It is upon this approach to the problem that I propose to concentrate.

Non-medical Manuscripts

The oldest picture of goitre or cretinism that I have yet discovered is to be found in Codex 507 of the Austrian National Library in Vienna, i.e. in the so-called "Reuner Musterbuch". This codex, dating from 1215, emanates from the Cistercian Abbey in Reun near Graz in Styria, a region in which goitre is still highly endemic to-day. It depicts a remarkable figure, with three large goitres and a stupid facial expression,

[1]Unfortunately it is not possible to reproduce here the full text of the lecture and the many illustrations which accompanied it. The material omitted here will be included later in a publication on the history of endemic goitre and cretinism.

brandishing a fool's staff in one hand and reaching up with the other hand towards a toad (Fig. 1). Most of the drawings in the "Musterbuch" (or "Book of Samples") were made as sample designs for the "Physiologus", a moralizing bestiary dating back possibly as far as the third century A.D. The drawings of various animals contained in folio 9^{v} are still completely imbued with the traditional, unrealistic style of the twelfth century. It is hence all the more striking that the cretin should have been depicted so realistically. This is, in fact, an example of the sporadic emergence of a progressive, more naturalistic form of portrayal which art historians have observed in the thirteenth century.

FIG. 1.—Cretin with three goitres from the "Musterbuch" from Reun. 1215. Austrian National Library, Vienna. Codex 507.

The Cistercian Abbey of Reun is situated in Styria, a region in which goitre had undoubtedly been endemic for many centuries. The first reference to goitre in Styria dates from the sixteenth century (Sebastian Münster, 1530), but as early as 1240—in other words, about the time the Reun drawings were made — Bartholomæus Anglicus mentions that goitre was very common in the neighbouring land of Carinthia. The question as to why the artist placed a staff or cudgel in the cretin's hand can only be answered as follows. The cudgel represents the old mimical chastizing rod which was the classical attribute of the fool in the Middle Ages. The iconography of the fool from the thirteenth to fifteenth centuries is well illustrated in illuminated psalters. The 52nd psalm opens with the words: "Dixit insipiens in corde suo non est Deus". The fool is accordingly often depicted in the initial letter D and always with a cudgel. But why is the cretin grasping at a toad? Frogs and lizards already played a major role in popular medicine in classical times (cf. Pliny), and even more so during the Middle Ages when one popular remedy for goitre consisted in binding live or dismembered frogs to the goitre. In the first half of the fourteenth century John de Gaddesden, a London physician, claimed to have won a prize from the London Barber Surgeons' Guild for a prescription of which tree-frogs were the main ingredient. In 1514, Giovanni Vigo, an eminent Roman physician in the service of Pope Julius II, concocted a so-called "Emplastrum de ranis" which still figured in the London Pharmacopœia of 1618!

And now, a final word as to the importance of the Reun cretin in the history of medicine. It is the earliest pictorial document bearing witness to the occurrence of goitre and cretinism as an endemic disease in the Middle Ages, and it anticipates by some 300 years the discovery that goitre and cretinism go hand in hand. Paracelsus is repeatedly acclaimed as the discoverer of the relationship between goitre and cretinism; but it may well be that the artist of Reun was already aware of the connexion 300 years earlier. Incidentally, after Paracelsus almost another three centuries were to elapse before this notion became established as a scientific fact.

Two very important sources of literary documentation on endemic goitre and cretinism in the thirteenth century are the encyclopædias of Jacques de Vitry and Thomas of Cantimpré, which record fables of human monsters extending back to Greek authors, to Greek and Indian mythology, to the Physiologus, and to the bestiaries of the Middle Ages.

In the thirteenth century an event occurred for which the historian of goitre has every reason to be grateful: one of the encyclopædists decided not only to reproduce the traditional series of fantastic monsters, which by that time was already some 1,500 years old, but to add to these monsters descriptions of giant goitres based on authentic observations "in extremis Burgundiæ circa Alpes". For this we have to thank Jacques de Vitry, a much-travelled itinerant preacher who had participated in the Crusades. During his travels he must have crossed the Alps on several occasions, probably by way of the Great St. Bernard Pass. In chapter 92 of his "Historia orientalis" (1220) a particularly interesting passage is to be found. After the usual list of human monsters (giants, pygmies, skiapods, acephali, &c.) in India, i.e. in the East, he reverts to the West and writes: "In quibusdam regionibus et maxime in extremis Burgundiæ circa Alpes

quædam sunt mulieres guttur magnum usque ad ventrum protensum tanquam amphoram seu cucurbitam amplum habentes." He continues: "Quidam autem tantas in dorsis habent strumas [meaning not a goitre, but a hump on the back!] quod quidquid in augmentum corporum cedere debet, gibbus absorbet et propter hoc parvi sunt vel nani . . . Ex mutis et surdis, muti et surdi infantes procreantur". Thus, here, along with non-existent, fabulous monsters, genuine human monsters have suddenly been included because of their giant goitres and cretinous deformities.

Twenty years later (1240) in his own encyclopædia, Thomas of Cantimpré, a pupil of Jacques de Vitry, reproduced word for word the descriptions of human monsters and the report on giant goitre and cretinism "in extremis Burgundiæ circa Alpes" which figure in his master's work. The encyclopædia of Thomas of Cantimpré was translated into various languages and many of the manuscripts were probably illustrated, although very few of them are still extant.

This brings us to a series of *pictorial representations of goitre*, which, once again, made their appearance long before pictures of goitre in medical literature. The few illustrated manuscripts of Thomas's "De monstruosis hominibus" that are still preserved doubtless originated from regions free from goitre. It is therefore interesting to see how the artists who illustrated these manuscripts portrayed goitres, having probably never seen any themselves.

Illustrations from two fourteenth century manuscripts (Paris, The Hague) are reproduced here (Figs. 2 and 3).

FIG. 2.—Woman with "giant goitre". Illustration to Thomas of Cantimpré's "De monstruosis hominibus". Bibl. Nat. Paris. Ms f. français 15106. Fourteenth century. Photo B.N.

FIG. 3.—Jakob van Maerlant "Der naturen bloeme", including Thomas of Cantimpré's "De monstruosis hominibus". Royal Library Den Haag. Codex XVI. Second half of the fourteenth century.

A French version of Thomas's encyclopædia was also extraordinarily widely read, i.e. the "Imago mundi" of Gossouin (1246). I should like to mention here only his reference to "Burgundian goitres", which runs as follows: "Du côté du Mont-Gieu femmes qui ont sous le menton des grosseurs qui leur pendent jusqu'aux mamelles: c'est considéré une beauté. Bossus, tordus comme des crosses, muets, sourds, hermaphrodites, gens qui naissent sans pieds et sans mains." Here, for the first time, the geographical location of the endemic is more specific: "Mont Gieu", derived from the Latin "Mons Jovis", is known to-day as the Great St. Bernard Pass. I have examined many manuscripts of Gossouin's "Imago mundi" in various libraries. Unfortunately they show no illustrations of the monsters.

Konrad von Megenberg is thought to have been the first natural historian to write in the German language. In his "Buch der Natur" (1349/50) he, too borrowed much from his predecessors, although he also incorporated into his work certain popular concepts, some observations of his own, as well as a great many moral exhortations. So far I have been able to discover only printed versions of his book, published one hundred years after his death. One of the most delightful features of the book is a large wood-cut illustrating the chapter on "wondrous men". It shows a number of naked figures wandering around—all of them fantastic monsters, including one

FIG. 4.—Konrad von Megenberg's "Buch der Natur" (1349). Printed edition of 1475. A woman with a big pendulous goitre among Indian monsters.

woman with a large pendulous goitre (Fig. 4). Here, in one and the same picture, we have concrete evidence to support the argument we have already discussed and corroborated, namely that a real phenomenon which the mediæval observer regarded as a monstrosity was therefore included by him in the same category as fantastic and fabulous Indian monsters.

In the middle of the fourteenth century we have yet another picture of a cretin with a goitre which is no less singular than the Reun cretin. It is the figure of an "insipiens" in the psalter of St. Lambrecht (Codex 387, University Library of Graz) ascribed to the year 1346 (Fig. 5). In the initial letter D of the 52nd psalm the "insipiens" (the fool) is depicted as an obvious cretin. His pasty face bears an infantile expression; he gives the impression of being a cautious, phlegmatic creature, and has clumsy hands and feet. In his left hand he holds a fool's staff with a pig's bladder attached to the top (this, like the cudgel, being a symbol of the "insipiens"). We cannot enter here into the history and iconography of the fool in the psalters of the thirteenth to fifteenth centuries, but in most of the initial figures to Psalm 52 he holds a round loaf in his hand and is depicted gnawing hungrily at it. In contrast to this, the St. Lambrecht cretin holds in the right hand his large twin-lobed goitre. Goitre and cretinism were widespread in Carinthia (as we have already seen with reference to Bartholomæus Anglicus, 1240) and also in the vicinity of St. Lambrecht. We can even determine with a fair degree of certainty the very name of the "insipiens" portrayed in the miniature. Listed in the necrology of St. Lambrecht in the fourteenth century is a certain Henricus Scheiterl, referred to as "fatuus valde mirabilis", in other words, as a remarkable simpleton.

Here, once again, it is not a physician but a monastic artist whom we have to thank for this valuable medico-historical document on endemic goitre and cretinism in the Middle Ages.

Another source of pictures of goitre is Boner's "Edelstein". In 1350 the Dominican monk Ulrich Boner completed in Berne his collection of fables known as "Gemme" or "Edelstein". It belongs to the category of collections of so-called "exempla", i.e. of "moralizing examples" which preachers in the thirteenth and fourteenth centuries were fond of using in their sermons. Of Boner's collection of 100 fables, the majority are taken from Aesop, a considerable number from Avianus, and the rest from various sources.

FIG. 5.—Psalter from St. Lambrecht. 1346. Cretinous "Insipiens" in the initial letter D of Psalm 52. Univ. Library of Graz. Codex 387.

FIG. 6.

FIG. 7.

FIG. 6.—Illustration to Boner's "Edelstein". Univ. Library Heidelberg. Cod. Pal. Germ. 794. About 1420.

←FIG. 7.—Illustration to Boner's "Edelstein". Univ. Library Heidelberg. Cod. Pal. Germ. 314. Dating from 1445.

FIG. 8.—Swiss illustrated chronicle of Tschachtlan, 1470. Bernese warriors killing their goitrous Vallaisan enemies by slitting their goitres.

FIG. 9.—Swiss illustrated chronicle of Diebold Schilling, 1484. The Vallaisans with their big goitres penetrating into Bernese territory. →

FIG. 8.

FIG. 9.

In his 76th fable, Boner tells the story of "The hunchback and the tollman":

In a certain small town, the count had the right to impose a "toll" on everyone wishing to cross the bridge into the town who happened to be suffering from some ailment. When a hunchback refused to pay the tax to the tollman for the hump on his back, a quarrel broke out; the two came to blows, during which the tollman discovered that the would-be tax-evader had four further ailments (goitre, blindness in one eye, favus, and scabies). Finally the hunchback had to pay 5 pence instead of the penny originally demanded. (The moral of the tale: it is better to pay small debts at once, lest they accumulate into bigger ones.)

Boner borrowed this story from Etienne de Besançon, but had the bright idea of giving the hunchback a goitre instead of the hernia from which Etienne's hunchback suffered. Whether he did this for "æsthetic" reasons is a matter for conjecture. At all events, in fourteenth century Berne Boner must have seen many cases of goitre and evidently regarded the disease as a common ailment.

Unfortunately, the oldest Boner manuscripts have been lost. Very few are illustrated. Only four of them—all from the first half of the fifteenth century—contain an illustration of fable 76. Three show the hunchback's goitre, thus serving as further pictorial documentary evidence of endemic goitre at that time (Figs. 6 and 7).

The three hunchbacks with goitres figuring in manuscripts from the first half of the fifteenth century (Basle, Heidelberg) provide documentary proof of the existence of endemic goitre at a time when the very first, and far more primitive, sketches of goitre had only just begun to appear in medical literature.

The iconography of the Swiss chronicles of the last quarter of the fifteenth century is, of course, far inferior to the splendid illustrative art found in contemporary English, French, Flemish, and Italian sources. Its quality is determined by the amateurish technique of the artists, one of whom (Tschachtlan) was a historiographer and the other (Diebold Schilling) a judicial clerk. Nevertheless, these chronicles are of interest, since they contain many illustrations of goitres. These artists evidently took a delight in depicting minute details of the events described in them (consisting largely of raids carried out by Bernese and Vallaisan warriors in the fourteenth and fifteenth centuries), and their chief motive for introducing goitres was to poke fun at the victims of the disease—a fact which explains why the Bernese artists portray the Vallaisans, and only the Vallaisans, with goitres! Here, for the first time in manuscripts, we have goitres depicted for the purpose of making the individual appear despicable and ugly, a phenomenon by no means rare in paintings and sculptures of this period.

In Figs. 8 and 9 can be seen a number of these goitrous Vallaisans. In the foreground of one of the drawings a Bernese warrior is slitting the throats or, more precisely, the goitres of his enemies. This, incidentally, serves as a reminder that in the Middle Ages the goitre was apparently regarded as a particularly vulnerable spot and was accordingly singled out for special attention during a fight.

"*Goitre Illustrations*" *in Medical Manuscripts of the Fifteenth Century*

Now that we have seen several quite impressive pictures of goitres and cretins from non-medical manuscripts of the thirteenth to fifteenth centuries, let us take a brief look at medical manuscripts. We have to start as late as the fifteenth century, since no goitre illustrations of earlier date have been found in medical manuscripts. Knowledge of anatomy in the Middle Ages was very limited, and anatomical illustrations were remarkably late in appearing. Perhaps one reason is that mediæval physicians derived their knowledge of Greek medicine via the Arabs, who were forbidden to make illustrations of human figures: As a result, in the course of the centuries the medical profession possibly made a virtue of necessity and was content to manage without the aid of pictures. With regard to anatomical illustrations, the well-known medical historian Diepgen writes

FIG. 10.—"Wound-man" (detail) with two "struma", one proceeding from the œsophagus, the other adjacent to the trachea. Paris, Bibl. Nat. Ms f. lat. 11229. Beginning of the fifteenth century.

Photo B.N.

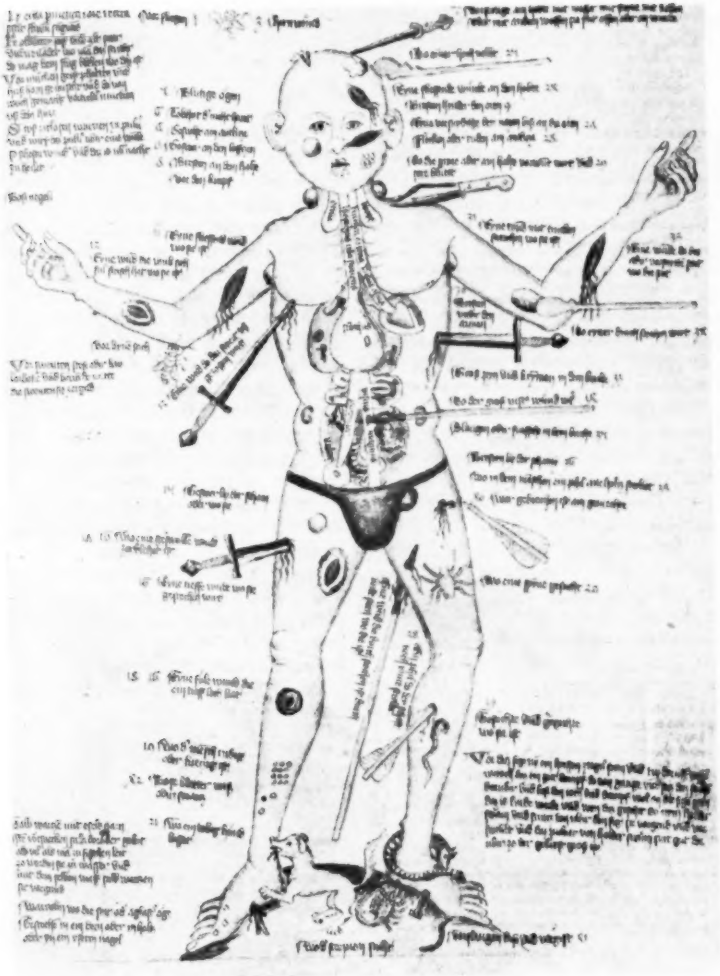


FIG. 11.—"Wound-man" with a "struma" and a "kropf" close to the œsophagus and to the trachea. Wellcome Apocalypse manuscript, dating from about 1460.

as follows: "It is one of the most peculiar phenomena in the history of medicine that in anatomy . . . two whole centuries were to elapse before a correct conception of the structure of the human body was evolved . . . Often the artists merely drew a brief *outline*, a sort of symbol, leaving it to the reader to figure out what it was meant to convey" (cit. from Fleck).

The only pictures of goitres that I have so far succeeded in finding in medical manuscripts of the fifteenth century are all drawn in this curious schematic fashion. One has indeed the impression that the physician of those days was satisfied with primitive diagrammatic outlines.

All these pictures originate from so-called "precursors" of Ketham's "Fasciculus Medicinæ" the first edition of which appeared in Venice in 1491. This work contains a woodcut of a "wound-man", a figure adopted from earlier drawings in manuscripts and presenting a pictorial review of the various injuries which the human body is liable to sustain. From head to foot the naked

figure is covered with every conceivable form of injury, together with a few externally visible diseases.

The oldest of these "precursor" figures appears in a manuscript in the Bibliothèque Nationale in Paris (Ms lat. 11229). It is a diagrammatic drawing, dating from the beginning of the fifteenth century. Particularly interesting are the two tube- or sac-like excrescences on the neck, both of which are marked "struma". The one on the right leads from the œsophagus, from which it bulges outwards. The one on the left lies adjacent to the trachea (Fig. 10). The artist seems to have made a mistake here: according to Greek authors, goitre was supposed to be a protrusion from the windpipe ("bronchocele"), whereas here the artist has shown it proceeding from the œsophagus!

In the "wound-man" of the Wellcome Apocalypse manuscript, dating from about 1460, there are once again two pouches next to the trachea and œsophagus which are marked "struma" and "kropf" (Fig. 11).

The two "wound-men" depicted in manuscripts in Munich and Copenhagen both show goitres on the right side of the neck.

These are the only goitre illustrations I have found in medical manuscripts produced prior to the year 1500. This paucity of material is all the more remarkable since—during the last quarter of the fifteenth century in particular, at least in areas where goitre was endemic—many goitres appear in both painting and sculpture, bearing witness to the vivid, realistic, and often grotesque style of Late Gothic art.

To sum up: the non-medical manuscripts of the thirteenth to fifteenth centuries that have been discussed and the illustrations contained in them serve as documentary evidence for the existence of goitre and cretinism as an endemic disease at a time when medical manuscripts still shed no light on this subject. They also indicate the localities to which these endemics were confined. The encyclopædias of the thirteenth century (Jacques de Vitry and Thomas of Cantimpré) were very widely read. Hence, knowledge of the existence of the goitre and cretinism endemic in the region of the Great St. Bernard Pass must also have been very widespread in the Middle Ages. That medical authors ignored it must be ascribed to the fact that "giant goitres" were included in the same category as the fabulous monsters of India and therefore seemed incredible to them. Compared with the numerous pictures of goitres to be found in non-medical manuscripts of the thirteenth to fifteenth centuries, the few primitive, diagrammatic sketches of goitres which first began to appear in medical manuscripts of the fifteenth century cut a very poor figure. Illustrations in medical manuscripts simply failed to keep pace with the flourishing art of the Gothic and Late Gothic period.

Meeting
September 29, 1960

Meeting in Connexion with the First British Congress on the History of Medicine and Pharmacy

The following papers were read:

The Influence of Health Insurance Schemes—Dr. Ffrangcon Roberts.
The Influence of Medical Societies—Dr. W. H. McMenemey.
The Influence of Clinical Research—Dr. K. D. Keele.

The papers will be published in "Evolution of Medical Practice in England", under the editorship of Dr. F. N. L. Poynter, during 1961.

Section of Obstetrics and Gynæcology

President—H. J. MALKIN, F.R.C.O.G.

Meeting
May 27, 1960

Gynæcological and Obstetrical Impressions of a Visit to the United States

[*Abridged*]

By FRANK MUSGROVE, M.D., F.R.C.O.G.

London

IT would be impossible to describe adequately the warmth of the welcome and the inexhaustible hospitality that our American colleagues shower so lavishly on any British doctor who cares to visit them. And, what a great experience it was to see their wonderfully equipped departments and to discuss with them views—both old and new—on matters of obstetrical and gynæcological importance.

Obstetrical Impressions

First, the more frequent resort to *surgical induction of labour*. Indications for induction are many, and may be considered under two main headings: (1) Induction of convenience, often called elective induction of labour: By this is meant that, towards the end of pregnancy the patient is actually given a date on which to enter hospital for her membranes to be ruptured. Such a date is usually convenient both to the patient and to the obstetrician. (2) Induction of necessity: Indications in this group are the usual ones, such as pre-eclampsia, post-maturity, diabetes, &c.

The induction itself consists in a low surgical rupture of the membranes and immediately an oxytocin drip is set up and given continuously throughout the whole of the first, second and third stages of labour. Even after the placenta has been delivered, if any infusion still remains, it is run in as fast as possible until it is finished. Indeed, the American obstetrician does not share the British fear of oxytocics which are given as freely to multigravidæ as to primigravidæ.

Rupture of the hind-waters and pure medical inductions, as we know them, are rarely, if ever performed.

Post-maturity, a well-recognized and feared condition, is divided into two groups: (1) Absolute post-maturity, which is considered to have occurred if, after reaffirming the expected date of delivery by a careful re-checking of the patient's menstrual history, some or all of the following signs are present: (*a*) Diminution in the amount of liquor amnii. (*b*) Engagement of the fœtal head. (*c*) X-ray evidence of maturity. (*d*) Cervical maturity, the "ripe" cervix. (2) Post-dated maturity when, in the absence of the above signs, the patient is not considered to be post-mature but merely to have exceeded her expected date of delivery.

Pain-relieving drugs in labour.—At present pethidine is much less commonly used than it is here, and barbiturates by mouth, especially Nembutal, were the drugs of choice. But in all primigravidæ and in most multigravidæ some form of extradural or fractional caudal analgesia is set up when the cervix becomes 2 to 3 fingers dilated. As a result, the rate of forceps deliveries is considerable, but whether or not forceps are used an extensive prophylactic episiotomy is carried out in *all* cases.

Progress in labour.—When a vaginal examination is carried out to assess the degree of descent of the fœtal head, the level at the ischial spines is the index, and if the head is at this level it is said to be at zero station. If the head is above or below this level then the distance is measured in centimetres and the head is said to be at zero station minus 1, 2, 3 or 4 cm if above the spines; alternatively, zero station plus 1, 2, 3 or 4 cm if below. Thus zero station −4 cm indicates a free head; zero station +4 cm a "crowned head".

Cæsarean section.—American obstetricians tend to turn to Cæsarean section more readily than we do, and the old adage "Once a Cæsarean section always a Cæsarean section" is still strongly held.

Afibrinogenæmia and hypofibrinogenæmia.—Increasing attention is being paid to the fibrinogen content of the maternal blood, more especially in the following conditions: (1) Missed abortion. (2) Hydatidiform mole. (3) Intra-uterine death, the so-called dead fœtus syndrome. (4) *Severe* accidental hæmorrhage.

If blood-clotting times are found to be increased, fresh blood transfusions, intravenous fibrin and intramuscular vitamin K are immediately given, and spontaneous onset of abortion

or labour is encouraged rather than induction in these cases.

Modern diagnosis and treatment of pre-eclampsia.—As a guide to the clinical cause of pre-eclampsia, particular attention is paid to (*a*) The fundi, for early signs of vasospasm. (*b*) A relative rise, first in the diastolic, and later in the systolic blood pressure, or over 20 mm Hg. (*c*) The pulse pressure, for should this be much greater or much less than one-third of the systolic pressure this finding should serve as a serious warning signal.

Treatment, as in this country, is directed to adequate antenatal care; a low sodium, high protein, high vitamin diet; mild sedation, and to the use of hypotensive agents, particularly the rauwolfia groups of drugs, usually in combination with diuretic drugs of the benzothiadiazine series.

Whereas in this country emphasis is laid on the importance of heavy sedation in the treatment of eclampsia, in America the aim is to reduce the hypertension as quickly as possible and to empty the uterus at the earliest opportunity. Morphia is rarely used since it is considered that the complications resulting from respiratory depression are more likely to prove fatal than the fits themselves. Barbiturates are again the drugs of choice to produce moderate sedation and the patient's stomach is kept empty by continuous gastric suction. One startling piece of research was under way when I visited the George Washington Hospital in Washington and that was the treatment of eclampsia by the hypothermic-hypotensive technique. Briefly, this was as follows:

Each eclamptic patient, on admission, was placed on a water-mattress through which ice-cold water was circulated. A thermocouple was inserted in the rectum for continuous temperature recording, and the urinary output was measured from an indwelling catheter. Whilst the cooling process was in progress an intravenous drip of 5% glucose was set up, to which were connected two infusions—one containing a powerful hypotensive drug trimetaphan and the other of Neosynephrine.

The hypotensive drip was administered to cause a steady fall in blood pressure, and then to maintain a systolic pressure between 90 and 100 mm Hg. In the event of a sudden drop in blood pressure this drip was stopped and the Neosynephrine solution substituted.

When the rectal temperature reached 34° C (average time taken two hours) the patient was moved to the operating theatre for vaginal delivery or Cæsarean section.

After delivery, rewarming of both the mother and baby was allowed to proceed *spontaneously*, without the application of any external heat. The "refrigerated" babies, born with respirations of only 3–4 per minute, were of good colour and the fœtal heart-rates were within normal limits. The hypotensive therapy was continued but gradually diminished until the blood pressure stabilized to within normal limits.

10 patients had so far been treated by this method. 2 had had vaginal deliveries and 8 underwent Cæsarean section. All 10 mothers survived and so did their babies.

Gynæcological Impressions

At all the bigger gynæcological centres it would seem that the present-day trend in gynæcological surgery is to remove the pelvic viscera, whenever possible, *per vaginam*. Certainly, vaginal hysterectomy is by far the commonest operation seen, and its use is by no means limited to the treatment of prolapse with or without functional uterine hæmorrhage. Indeed, even when the uterus is considerably enlarged with fibroids, and often in the *absence* of prolapse a vaginal hysterectomy together with morcellement of the fibroids, is the operation of choice.

Even ectopic pregnancies and certainly most operations for sterilization are commonly tackled through a wide posterior colpotomy, and where necessary the uterus is retracted backwards and downwards to be partially withdrawn through this incision.

In defence of this trend towards vaginal surgery may be offered the following points: (*a*) This approach causes considerably less post-operative discomfort and is more conducive to early ambulation. (*b*) The patient's stay in hospital is considerably reduced. (*c*) Most women would prefer to have an unseen dimple in the vagina than a large and often unsightly abdominal scar.

Chronic pelvic infection and diffuse endometriosis—two conditions which appear to be extremely common in the United States—seem to be the only contraindication to vaginal surgery, and their presence is usually excluded beforehand by culdoscopy, a very common preoperative procedure in America but one which has found little favour in this country.

Possibly as a result of so much vaginal surgery, the demand for blood transfusions is considerable. Indeed, each patient undergoing a gynæcological operation, other than a straightforward dilatation and curettage, has an intravenous glucose-saline drip set up preoperatively so that the changeover to a blood transfusion can be quickly effected if necessary.

American surgeons are placing increasing reliance on scientific methods for deciding

whether or not a transfusion is indicated. One procedure now in common use is called tagged red-cell assessment, whereby a known amount of radioactive chromium isotope is injected intravenously before the operation is commenced. This isotope becomes attached or "tagged" to the red cells and some minutes later a sample of blood is withdrawn. After operation a further sample is taken and the concentration of isotope in the respective samples is measured by the radiation recorded on a Geiger-Müller tube. Then, by using a somewhat complicated formula, the total blood volumes are assessed. The difference in pre- and post-operative assessments is then the guide as to whether or not replacement therapy is indicated.

Recovery rooms.—On each theatre floor there is a large recovery room. This so-called "room" is, in fact, a fully equipped resuscitation ward of some 6–12 beds to which all patients are transferred immediately after operation, and where they remain until they are *fully conscious*.

Each recovery bed, which can be raised, lowered, tilted in any direction or angle, &c., is separately equipped with: (1) An oxygen tent. (2) Piped oxygen and carbon dioxide. (3) A continuous suction apparatus. (4) A sphygmomanometer. (5) An electrocardiographic machine, and (6) A resuscitation trolley containing all the necessary stimulants together with a complete set of instruments needed should cardiac massage be called for.

Each recovery room is manned round the clock by shifts of specially trained nurses.

Prevention and treatment of paralytic ileus.—Recently a drug called d-pantothenyl-alcohol, known in England under its proprietary name of Bepanthen, has been revived and used with considerable success in the prevention and treatment of post-operative paralytic ileus. Bepanthen, a factor of the vitamin-B complex, plays an essential part at the autonomic ganglion and post-ganglionic parasympathetic nerve endings to ensure normal intestinal motility. In most abdominal operations and even in labour, particularly a long labour, the metabolism of pantothenic acid is often seriously interfered with and atony of the *bowel*, and sometimes of the bladder, may ensue. Prophylactically, 500 mg of Bepanthen is given intramuscularly immediately after operation and repeated at six-hourly intervals for the first twenty-four hours.

In the treatment of ileus, its use is continued up to forty-eight or seventy-two hours, and longer if necessary. In the more severe cases it is combined with "drip and suction", but usually these latter measures are less frequently required, and the length of time they need be continued is considerably reduced.

No medical trip to the United States is complete without a visit to the National Institutes of Health Hospital, just outside Washington. It is made up of a number of institutes or centres which carry out research in *all* branches of medicine. The building has 500 private rooms and each room has a fully staffed and fully equipped laboratory on either side of it! Patients occupying them pay no hospital or medical fees, but agree to undergo any examination, tests or treatment that might be embarked on. Each patient has two doctors to himself, and these doctors, paid by the Government, devote their entire time to the investigation and treatment of the disease of that particular patient.

During my visit to the National Cancer Institute the most astounding research I saw was in the treatment of chorionic cancer and allied conditions, including hydatidiform mole, with the folic-acid antagonist methotrexate, by Dr. R. Hertz and his co-workers. Their treatment consists in the administration of methotrexate, usually intramuscularly but sometimes by a continuous intravenous drip, in daily doses of 10–30 mg for five days. The average period of time occupied by a given five-day course was twelve days (some patients became toxic, and the drug had to be omitted sometimes on alternate days); the average number of five-day courses per patient was 6; and the average total dose of methotrexate per patient was 620 mg.

The aim is to hit the disease hard with the first few courses, for whereas all tumours appear to be initially responsive, a few become methotrexate-resistant. One great drawback to this therapy is that some patients may develop severe toxic reactions which include stomatitis, intestinal irritation, skin eruptions and depression of bone-marrow activity.

Response to treatment is assessed by (1) improvement in the patient's general condition, (2) radiological evidence of diminution and ultimate disappearance of secondary deposits—commonly in the lungs and bones, and (3) a fall to normal limits in the urinary excretion of chorionic gonadotrophic hormone.

The results of this treatment are reported by Dr. Hertz (personal communication, 1960) as follows: "We have now a total of 44 cases . . . in which 21 are in total remission; 14 are dead after partial remission and recrudescence of disease, and the remainder still in partial remission. Remissions have been as long as four years to six months. All but one case showed initial response to the drug."

Uteroplasty in Infertility

By MARGARET MOORE WHITE, M.D., F.R.C.S., F.R.C.O.G.
London

THIS paper is presented to emphasize the association of minor uterine abnormalities with habitual abortion, premature births, stillbirths and complications of labour. Palmer (1953) has placed the incidence of malformations in habitual abortion as high as 25%, Jones and Jones (1953) give a figure of 33%. Steinberg (1955) showed that two or more abortions occurred in 34·5% of cases, 1 or more premature births in 11·2% and sterility in 10·3%.

The minor abnormalities concerned are, using Jarcho's classification (1946), uterus unicollis bicornis, uterus septus, subseptus and arcuatus (Fig. 1). Steinberg (1955) mentions that the bicornuate uterus is less likely to account for complications than the septate. The bicornuate uterus may be detected on pelvic examination but the other varieties are rarely discovered and therefore hysterography should be a routine procedure in the investigation of habitual abortion. The malformations may be missed unless the uterus is examined under the screen and positioned in the frontal plane. If routine screening is not carried out and the uterus is markedly ante- or retroverted the abnormality may likewise be missed but may be suspected if the transverse diameter of the uterus is wider than usual. If screening is not available a film may be taken with the patient in the oblique-lateral position or the table may be tilted to bring the uterus into a plane that will demonstrate the deformity.

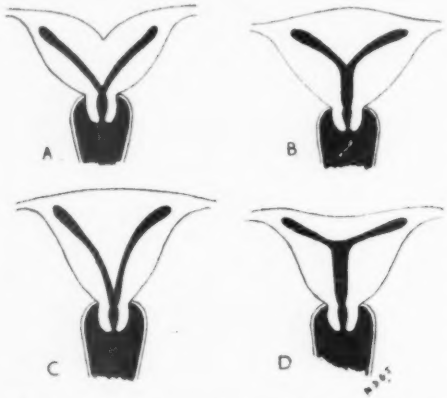


FIG. 1.—A, Uterus bicornis. B, Uterus subseptus. C, Uterus septus. D, Uterus arcuatus.

Although the majority of women with minor uterine abnormalities do not abort, there is an increased chance of malpresentation and fœtal loss. Jones *et al.* (1956) refer to an incidence of 17 stillbirths, premature stillbirths or neonatal deaths in 66 pregnancies and Hay (1959) refers to the probable incidence of 10% of women with minor degrees of uterine abnormalities in relation to pregnancy. It appears from their observations that the above-mentioned abnormalities account for many instances of premature births and stillbirths and for the necessity for the application of forceps or Cæsarean section with a raised fœtal loss. The reason for this is that the deformity causes a breech or transverse presentation.

Steinberg (1955) remarks on the incidence of dysmenorrhœa in 40% of cases. Murray (1926) and Strassman (1952) mention the association of these malformations with polymenorrhœa and the latter also stresses the high incidence of postpartum hæmorrhage.

Why should uteroplasty improve the chances of carrying to term? Strassman (1952) estimates that "by providing a breeding space twice the size the chances of carrying to term are more than quadrupled and the chances of miscarriage lessened by more than a fourth". Masters *et al.* (1957) suggest that not only does the uterus fail to respond to the tremendously rapid expansion and hypertrophy needed but are also of the opinion that an insufficient amount of progesterone is produced and they demonstrated pregnancy carried to term after administration of progesterone. Jones and his colleagues (1956) found that many of the women in their series showed evidence of metabolic or endocrinal defects and that pregnancy often carried to term after correction of these defects.

Failure to nidate and habitual abortion may be the result of the poorer blood supply to the endometrium via the septum. When the uterus has only one cavity, each side receives its blood supply directly from the uterine artery. When there are two cavities, either complete or partial, the fibromuscular septum receives an indirect blood supply from the uterine artery. The excised fibromuscular septum was examined histologically in 7 of my cases and in 4 of these the pathologist reported an excess of fibrous tissue. This would not only result in a poorer blood supply to that part of the uterus supplied via the septum but would also tend to bring about uneven and inadequate expansion of the uterus. The poorer blood supply may also explain the frequent association with an inadequate luteal phase since poorly nourished cells do not function so well.

There is a tendency for the woman with a divided cavity who aborts to carry longer in successive pregnancies ending in the delivery of a live child. Such a case was described by Ariel (1955).

When deciding on uteroplasty many factors should be taken into consideration: the age of the woman, the degree of malformation, although the woman with the less severe malfcrmation may repeatedly abort, her ability to face repeated disappointments and her husband's sufferance.

Uteroplasty is not usually associated with complications. Strassman (1952) collected 128 cases with no history of rupture during pregnancy or delivery and only one maternal death. Pregnancy is not advised until three months after operation. The question of delivery by Cæsarean section requires careful consideration in each case. In a survey made by Steinberg (1955) more babies were delivered *per vaginam* than by Cæsarean operation and there are many reports of women undergoing successful delivery at term. Operation was performed for 2 or more abortions in 37 cases in his series of which 16 had one or more live births.

Cæsarean section was carried out on the women who carried to term in my series. They were referred to the maternity unit in their own area for antenatal care and delivery. One woman died from heart failure complicating acute obstruction after Cæsarean section. The obstruction was probably due to a pelvic adhesion and was not a result of the Cæsarean section.

Strassman (1907) was one of the first to report successful reconstruction of a uterus with a divided cavity. He made a transverse incision across the fundus, cut out the septum and joined the two halves of the uterus in the sagittal plane in three layers, submucosal, muscular and peritoneal. Operators advocate apposition of the muscular layers with an interrupted non-absorbable suture of strong silk or nylon. Green-Armytage (1960) and Jones and Jones (1953) excise a wedge and join the two halves of the uterus in the sagittal plane in three layers as above. Seager Jones injects the cavity of the uterus with blue dye prior to opening the abdomen so that he may more easily distinguish the uterine cavity and this helpful procedure is worth following. Since the first operation performed in 1952 I have used a slight modification of this technique (Figs. 2 and 3).

A figure-of-eight suture is inserted on either side of the top of the fundus and held taut. An incision is made down the middle line until cavity is encountered. This sometimes extends as far as the cervical canal. An oblique incision is then made on one side to expose the cavity, but if not exposed by this incision a further cut is made, for sometimes the septum is very broad (Figs. 3 and 4). This procedure is then repeated on the

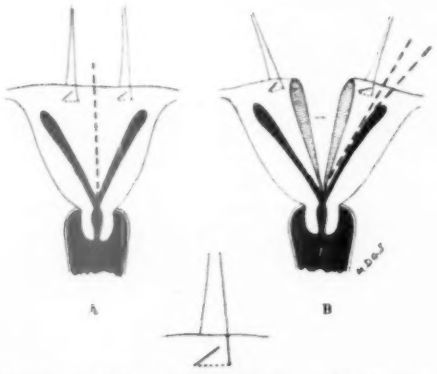


FIG. 2.—Technique of uteroplasty. A, Incision into fundus. B, Excision of wedge.

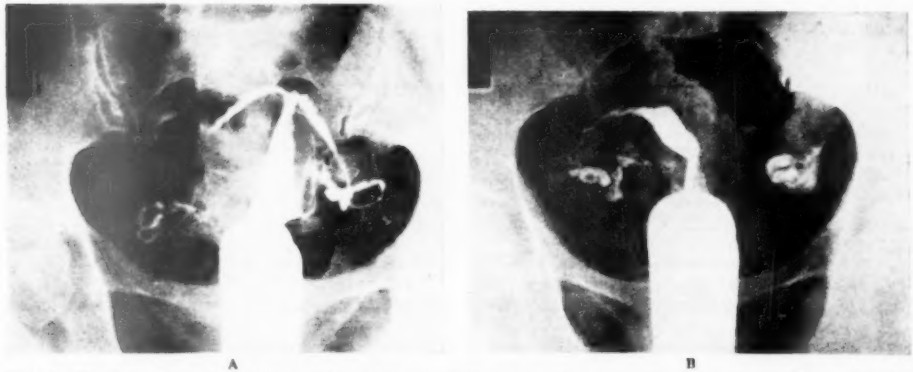
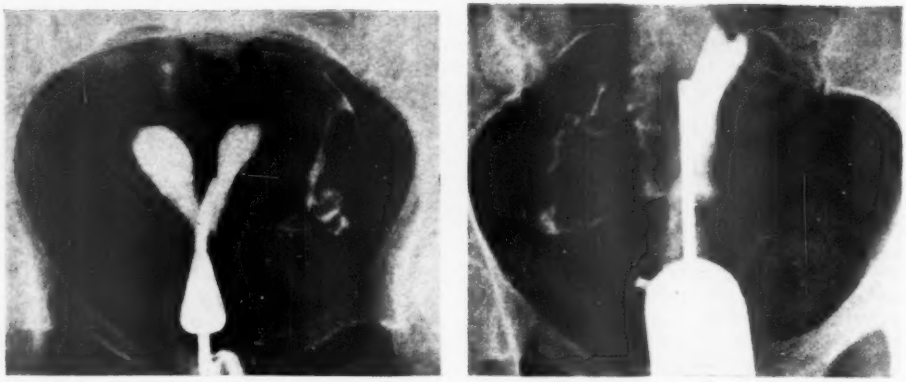


FIG. 3.—Septate uterus in extreme anteversion. A, before operation. B, after operation. On opening the abdomen the uterus appeared as a perfectly normal looking uterus, somewhat wider possibly than usual.



A B

FIG. 4.—Septate uterus. A, before operation. B, after operation.

other side. The two cavities are not necessarily of the same size and by the method described one ensures removal of as little normal tissue as possible. Since light adhesions to the scar have been visualized in 2 cases at the time of Cæsarean section, it is advisable to stitch an omental patch over the scar on the aspect that will come in contact with the intestines. In those cases in which the septum has extended to the cervix a uterine sound should be passed before the patient leaves the hospital to prevent cross adhesions.

In 2 cases in which the uterus has been notice-

TABLE I—RESULTS OF MODIFIED STRASSMAN OPERATION

Case	Age	Abortions	Malformation	Biopsy	Result	Comments
Group I: 3 or more abortions						
1	34	4 { 7 weeks, 8 weeks, 4 weeks, 4 weeks	Septate	Normal	Live birth	8 lb 12 oz infant 1 year after operation
2	26	3 { 6½ months died, 3 months, 2 months	Septate	Normal	Live birth	1st child, Cæsarean section at term. 2nd child spontaneous. Now 7 months pregnant, twins*
3	26	3 { 6 weeks, 3 months, 3 months	Septate	Normal	Live birth	8 lb child at term. Cæsarean section
4	36	5 { 6 weeks, 10 weeks, 12 weeks, 12 weeks, 12 weeks	Subseptate	Normal	—	Husband left her after operation
5	38	5 { 3 months, 3 months, 6 months, 7½ months stillbirth, 7 months died	Subseptate	Normal	Live birth	Cæsarean section at term, 6 lb 12 oz child. Mother died, post-operative acute obstruction followed by heart failure
Group II: 1 abortion						
6	39	1, 3 months	Subseptate	Normal	Abortion	Aborted at 3 months
7	29	1, 3 months	Deep subseptate	—	—	Cystic ovaries and septum discovered at D. & C. for incomplete abortion. Not tried
8	34	1, 3 months	Subseptate	Normal	Missed abortion	First conception preceded by salpingolysis and salpingoplasty †
Group III: sterility						
9	26	4 years sterile	Subseptate	Normal	Tubal abortion	L. salpingoplasty and bilateral salpingolysis performed at same time
10	29	4½ years sterile	Subseptate and hypoplastic	—	Live birth	Conceived after 3 months' trial
11	33	10 years sterile	Arcuate	Some anovulatory cycles	—	No conception yet after 4 months

*Since delivered spontaneously of twins. †Now 5½ months pregnant.

ably small œstrogens have been given in the early months of pregnancy to increase uterine growth. As soon as pregnancy is confirmed the woman is given 2·5 mg stilbœstrol daily, increasing the dose by 2·5 mg every two weeks until the 16th week of pregnancy when the dose is gradually reduced.

My series consists of 11 cases. In 7 the uterus was subseptate in type, in 3 septate and in 1 arcuate. They are classified in 3 groups (Table I): Group I, 5 cases with 3 or more abortions; Group II, 3 cases with 1 abortion; Group III, 3 women complaining of sterility. The operation was performed in the hope that the improved blood supply to the uterus would increase the chances of conception.

Summary.—5 of the women who underwent operation have conceived and their offspring survived, 1 had a missed abortion at the fifth month, 1 an early tubal abortion and 1 a three-month abortion. Owing to adverse domestic reasons 2 women have not had an opportunity to conceive and 1 has failed to conceive. Results suggest that the operation is justified after 3 or more abortions especially if the duration of pregnancy does not increase with each conception and no other cause for sterility can be found. An insufficient number of women complaining of sterility have undergone operation to be of statistical value, but if no other cause for sterility can be found uteroplasty should be considered.

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DISCUSSION

Mr. H. E. Reiss (London) said that reports of uterine rupture following Strassman operations were very rare in the modern literature. He knew of one such case, a young woman complaining of primary habitual abortions. Hysterosalpingography revealed a uterus bicornis bicorpus unicollis. A Strassman type of operation was performed; pregnancy occurred within three months. The uterus ruptured extensively at the site of the fundal repair at the 37th week, but fortunately the membranes remained intact, bulging through the wound. A living child was delivered (6 lb 1½ oz) through a separate lower-segment incision, and both uterine wounds repaired. A further pregnancy occurred one year later: this time the uterus ruptured at the 23rd week; it was again repaired, but tubal ligation was performed on this occasion.

Mr. V. B. Green-Armytage (London) emphasized that whatever the degree of arcuosity—very large or very small—there was always a fibromuscular wedge of tissue descending from a dimple on the fundus into the endometrial cavity and, as had been stressed by Falls of Chicago years ago, it was this wedge that was perhaps responsible for the abortions, and the deaths *in utero* of the fœtus from ischæmia of the placenta. That it was this wedge that caused the malpresentations, the retained placentæ and the cases of post-partum hæmorrhage. After two or three abortions or deaths *in utero* it was imperative to excise the wedge by a vertical incision and then just as in the case of a classical Cæsarean, as was shown in his classical monograph by Sir Eardley Holland one must use unabsorbable material such as nylon or SWG for the muscular layer of the uterus. If this rule was not remembered or obeyed then every young surgeon would from time to time have a ruptured uterus and dead child and maybe mother, if he used only catgut. During the last twenty years many registrars had shown and described such specimens at meetings of the Section.

Mr. John Stallworthy (Oxford) said that Mr. Green-Armytage had warned the younger surgeons present of the importance of technique in operating on uterine malformations. Mr. Stallworthy wished to add a note of warning with which he was sure both Miss Moore White and Mr. Green-Armytage would agree. It was of the need to retain a sense of perspective and not to imagine that every woman who was infertile or had had an abortion and was found to have a uterine malformation required surgical intervention. Miss Moore White was to be congratulated on the 80% success following her skilful surgery in her first group of 5 patients but world literature recorded a success rate of 80% in the treatment of habitual abortion by many different (and at times antagonistic) non-surgical techniques. It was easy to detect the uterine deformity in the infertile woman or after an abortion. It was also easy to forget that many women had their babies without difficulty in spite of uterine deformities. Plastic surgery undoubtedly had an important role to play (though a minor one) in the treatment of this condition but the clinician's greatest problem was to select the correct patient for surgery. It would indeed be a tragedy if young specialists were so impressed by the excellent results reported by Miss Moore White and Mr. Green-Armytage that they decided to operate on all abnormal uteri. Nature could also produce wonderful results if given a chance.

Miss Moore White, in reply to Mr. Stallworthy's comment that many women have their babies despite uterine abnormalities, said that she concurred with his view and had therefore suggested that operation should only be considered after three or more abortions, and provided that no other cause for recurrent abortion could be found.

DISCUSSION ON THE USES OF THE CARDIOPHONE IN THE LABOUR WARD

Mr. D. J. MacRae (London):

One of the main uses of the cardiophone in the labour ward is in early diagnosis of the abnormal heart action of fœtal distress. This entails a knowledge of the behaviour of the fœtal heart during labour. For instance, the heart-rate may quicken: (*a*) With fœtal movements. (*b*) During weak contractions, which stimulate fœtal activity, or cause, possibly, mild hypoxia and hypercarbia; the contractions of early labour are frequently associated with an increase in the heart-rate. (*c*) When, with failure of advance in the second stage of labour, because of strong pelvic muscles, or unruptured membranes, fœtal effort and stress are increased. (*d*) With rise in the maternal temperature.

The fœtal heart-rate may become slow and even irregular with anoxia due to: (*a*) Strong and prolonged uterine contractions; this is therefore a usual occurrence in the second half of labour. (*b*) Failure of the uterus to relax. (*c*) Compression of the umbilical cord. (*d*) Maternal hypotension (Hon *et al.*, 1960).

Irregular fœtal heart action and bradycardia may be caused by increased cerebral pressure, which may occur with a contracted pelvis, or at engagement of the head or by tight pelvic muscles and is typically relieved on release of the pressure.

Abnormal fœtal heart action, as frequently found in the second stage of labour, may be associated with analgesia and downbearing efforts, with their maternal cyanosis and placental stagnation from increased intra-abdominal pressure. The common gas and air analgesic when properly used is deficient in oxygen and, when improperly used, more or less continuously with shallow breathing, may cause serious oxygen lack, accentuated by respiratory depressants such as pethidine and by anæmia and impaired placental function.

Occasionally extrasystoles are present and may persist for some time after birth; and, rarely, there is abnormality of heart action, such as heart block, which is associated with congenital malformations or fibro-elastosis of the heart.

There are thus many reasons for changes during labour in the action of the fœtal heart, and its response will vary with the predominating influence; and since these changes may at first be intermittent interval recording may miss the abnormal phase and is inadequate as a safeguard. Continuous monitoring of the fœtal heart-rate has, therefore, a great advantage and (although not yet technically at the stage for use in all patients) is especially indicated in cases where fœtal distress and stillbirth are more common, including:

(1) Trial labour. In the presence of a contracted pelvis the fœtus is exposed to increased cerebral pressure, to abnormal uterine action and prolapse of the cord. Often a critical stage in the labour is reached when a further four hours will decide if Cæsarean section be necessary: here, continuous recording of the fœtal heart is both reassuring and helpful.

(2) Uterine inertia. When the blood supply to the placenta is impaired, especially in hypertonic uterine action, serious fœtal bradycardia may result. Again, by means of the cardiophone the fœtal heart can be recorded in a different room, while the patient is given an undisturbed and refreshing night's sleep.

(3) Insufficiency of the placenta (a descriptive term, well understood). With its blood supply affected, the fœtus, already enfeebled, may be unable to withstand the additional stress and hypoxia of labour. This group would include cases of pregnancy toxæmia, hypertension, postmaturity, Rh incompatibility, and those with a history of abortion or intra-uterine fœtal death. In the presence of this type of poorly functioning placenta gas and air should not be used.

(4) Elderly primigravid and subfertile patients require closer observation.

(5) Where temporary fœtal distress has already occurred—with heart changes or meconium staining of the liquor—further irregularity should be looked for.

(6) In the second stage of all labours (MacRae, 1959*a*). It is at this stage that abnormal fœtal heart action is most common and when the report often comes that the fœtal heart cannot be heard. It is here, therefore, that interval recording is most lacking. In the so-called normal case fœtal distress is common for such reasons as late diagnosis of the second stage of labour, or failure of the fœtal head to advance because of (*a*) tight pelvic floor muscles, (*b*) the unrecognized narrow subpubic arch which, especially in the absence of an episiotomy, arrests progress and leads to cerebral injury. As previously mentioned, expulsive maternal efforts may produce placental anoxia and analgesics cause reduced oxygen intake. It is also at this time that the umbilical cord when round the baby's neck may result in strangulation; as anoxia develops from this cause continuous heart recording would at once pick up the resulting bradycardia and immediate delivery could be undertaken.

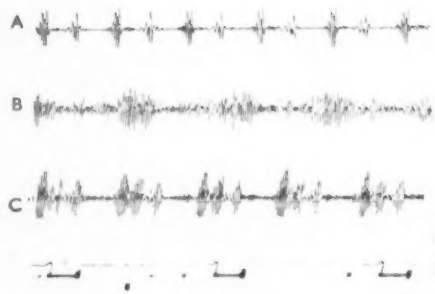

FIG. 1.—A, The fœtal heart, two sounds with each beat. B, The uterine souffle. C, The funic souffle. [Placings are read from right to left and have a one-second time marker.]

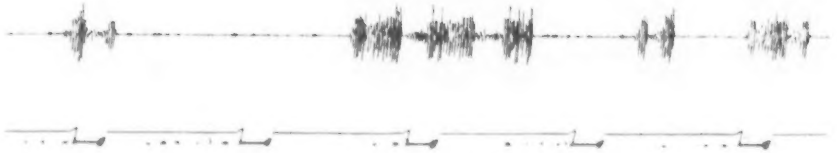

FIG. 3.—Fœtal head pushed into pelvis, heart slow and irregular.

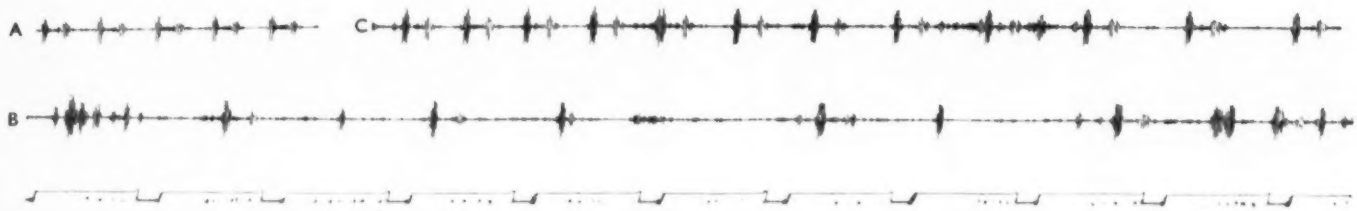

FIG. 2.—A, Occipito-posterior, fœtal heart before uterine contraction. B, Occipito-posterior, irregularity and slowing of fœtal heart during uterine contraction. C, Occipito-posterior, recovery of fœtal heart after uterine contraction.

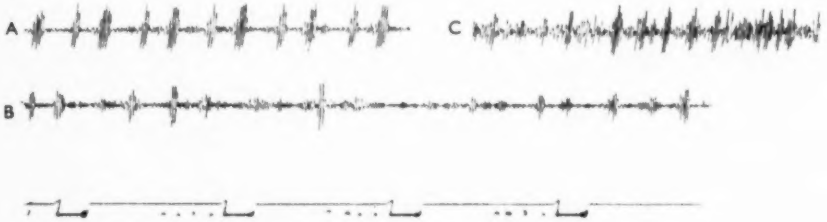

FIG. 4.—A, Delay on pelvic floor, fast fœtal heart. B, Irregular fœtal heart during forceps traction. C, Fast fœtal heart after release from forceps traction.

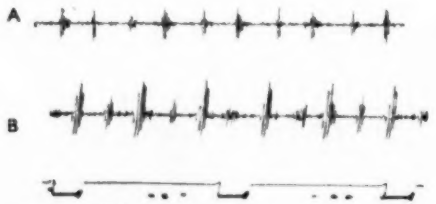

FIG. 5.—A, The normal heart in a baby 1 week old. B, Normal heart in a baby at birth.

FIG. 6A.—The baby has not breathed, slow heart of asphyxia.

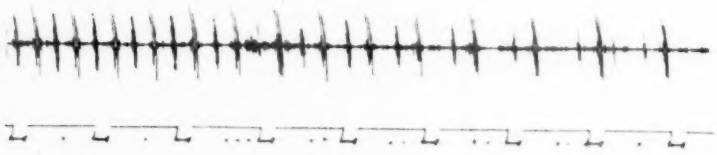

FIG. 6B.—With the first breath there is temporary recovery of the heart.

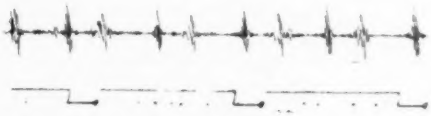

FIG. 6C.—The baby breathes and its heart recovers.

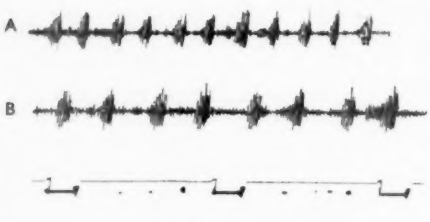

FIG. 7.—A, Exchange transfusion, increase in the baby's heart rate towards end of each injection of blood. B, Exchange transfusion, slowing of the baby's heart during withdrawal of blood.

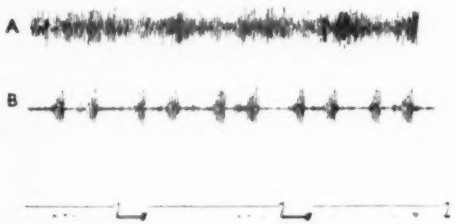

FIG. 8.—A, Patent ductus in a baby at 1 week. 8B, Patent ductus closed in same baby at 3 weeks.

The Baby

Recording by the cardiophone is simpler in the baby's heart. Its use in exchange transfusion makes this procedure less dangerous. In recent cases we found that this method revealed serious heart irregularity not suspected from the baby's appearance and we were thus able to modify treatment. Heart irregularity is especially liable to occur where the baby is premature or severely affected, or if there has been the additional shock of Cæsarean section. Usually an interval of six to twelve hours allows the heart to recover and further treatment can be given. It is a safe precaution to monitor the baby's heart in all cases for a few minutes before giving the transfusion and then to continue throughout.

In asphyxia the cardiophone has two parts to play. (1) At birth, when there is a general disregard for the behaviour of the baby's heart, heart monitoring provides a constant guide to the baby's condition and does not impede resuscitation efforts. (2) By helping to prevent during labour the prolonged fœtal anoxia which damages the vital centres. The immensity and urgency of this problem can be appreciated from a review of the causes of stillbirth. In a consecutive series of 100 stillbirths among our cases (from which ante-partum hæmorrhage, fœtal

abnormality, Rh incompatibility, cerebral hæmorrhage and prolapsed cord were excluded) atelectasis—with or without prematurity—was the only pathological abnormality found in 30. If a similar deduction could be made for the country as a whole it would mean that out of 19,000 (approximately) stillbirths which occurred in 1958 in Scotland, England and Wales 5,700 died with atelectasis the only abnormal finding. Such is the yearly magnitude of this problem, without taking into consideration neo-natal deaths from atelectasis and the late effects of anoxia.

I would, therefore, consider that, if fœtal distress contributes to stillbirth and asphyxia, closer study of fœtal heart action in both normal and abnormal labours would prove of immense benefit. Herein methods of continuous heart monitoring have much to offer.

Another important use for the cardiophone in the labour ward is in monitoring the fœtal heart beat during a Pitocin drip (MacRae, 1959*b*). (A film was shown to illustrate this procedure.)

Remote and continuous monitoring by this method permits the behaviour of the heart to be studied both during and between contractions and avoids repeated auscultation which causes apprehension and uterine inertia. This is a most necessary watch to keep, since common initial failure of the drip is often succeeded by more determined efforts.

Seven years ago Gunn and Wood projected the sounds of the fœtal heart from a loud speaker in this hall (*see* Gunn and Wood, 1953). When I brought a loud speaker into the labour ward, however, I found that interference from adventitious sounds and feed-back were greatly intensified. Fortunately, the basic heart sounds are in the low frequency range, even subsonic, and after much experimenting we were able to prevent feed-back by the simple device of raising the cardiophone sounds by an octave, so that when transmitted back through the microphone they were blocked by the Soniscope. As previously stated (MacRae, 1959*a*) we found that the microphone best suited for our purpose and the Soniscope with its pre-selection of sounds were those described by Kinnier Wilson, Fothergill, and Selwyn Taylor (1956). The sounds can be amplified by the Soniscope and by the cardiophone, especially when its sound trap is fully used.

The use of the cardiophone is shown from the phonocardiographic tracings (Figs. 1–8) taken from tape recordings (which were also demonstrated).

Acknowledgments.—The cardiophone was made for me by Faraday Electronic Instruments, Ltd., to whose staff of experts I gratefully acknowledge much pioneering help.

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Mr. Trevor Barnett (Portsmouth):

A New Type of Labour Ward Chart

The use of the cardiophone could undoubtedly reduce fœtal mortality because it measures accurately the fœtal heart-rate which is still the best means we have of recognizing fœtal hypoxia. But, by whatever means the fœtal heart-rate is counted during labour, this knowledge is of no value unless: (1) The observations are accurate. (2) The readings are properly recorded and seen in their relationship to the other significant phenomena of labour, such as progress of cervical dilatation, degree of descent of the presenting part, and presence or absence of meconium in the liquor. (3) If a graphic record of the labour is available, it is acted upon, and criteria of fœtal danger requiring expeditious delivery either vaginally or abdominally are agreed.

I have analysed 200 consecutive perinatal deaths at Saint Mary's Hospital, Portsmouth, during the two years 1957 and 1958. It can be clearly demonstrated that many of these deaths were due to neglect of these principles.

In order to remove these defects in observation and in recording, we have introduced a graphic method of charting the important details of labour.

The significant features of the system are: (1) The records are made as labour proceeds, and the charts, which run concurrently with the labour, are available at the bedside for inspection by the obstetric staff throughout. (2) Each observation is charted as it is made. (3) Conduct of the labour is based on the record on the chart and it is easy for anyone taking over the case to appreciate the course of the labour up to that time.

This is important, since it will be found that a number of avoidable stillbirths occur at week-ends, at times of change-over of duties from one obstetric firm to another, and at times when control of a patient passes from one set of resident staff to another.

Fig. 1 is a specimen chart showing record of a normal labour. On it are shown: (1) Hours of day or night with calibrations for each ten minutes. (2) Record of fœtal heart-rate. (3) Record of maternal pulse-rate. (4) Degree of

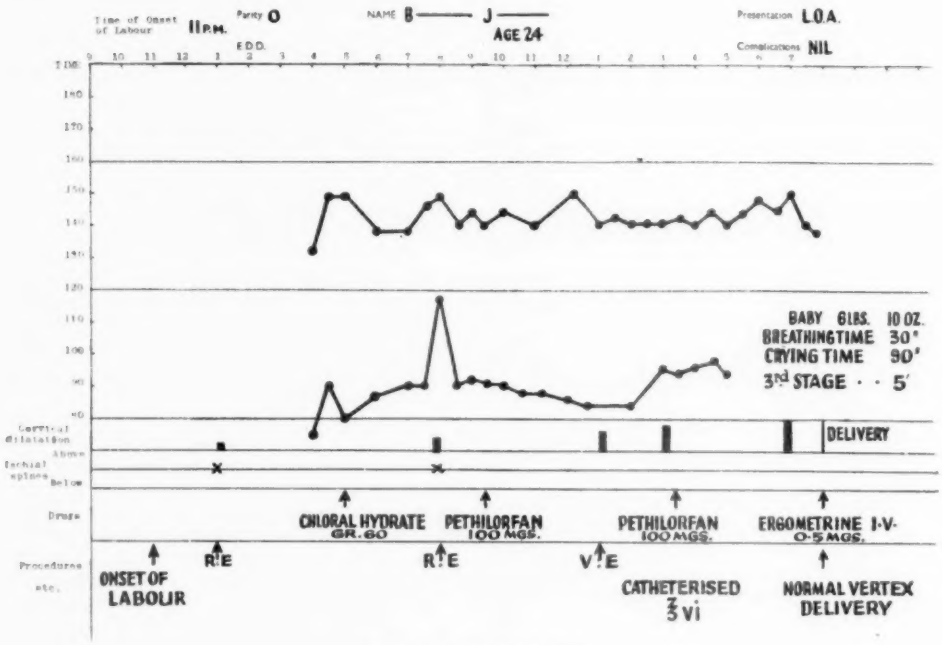

FIG. 1.—Labour ward chart.

cervical dilatation calibrated in notional finger-breadths. (5) Relationship of presenting part to the ischial spines—i.e. degree of engagement. (6) Space for entering details of drugs given. (7) Space for entering details of examinations or operative procedures.

Three special points may be mentioned: (1) There is no space on the chart for noting the time of appearance of meconium. We use a stamp which is impressed at the requisite point on the record. (2) There is no record of the uterine contractions. This is deliberate because the charts are based on objective findings and if fœtal distress is present, intervention must follow irrespective of the type of contractions which have preceded its onset. (3) A stamp is superimposed on the chart indicating when a re-assessment of the labour is necessary. This is used at the expiration of sixteen hours in the first stage. If labour is allowed to continue, another complete assessment must be carried out again sixteen hours later, when a definite decision is made as to whether the labour should be allowed to proceed to vaginal delivery or whether Cæsarean section should be carried out. This decision should be made after thirty-two hours of labour.

A cardiophone record incorporated in such a chart as this would be of great value in ensuring the accuracy of the record of the cardiac rate. The whole value of charts of this type must depend on the accuracy of the observations recorded.

Charts using the ideas here put forward would be instrumental in reducing stillbirth and neonatal death-rates. They would be particularly useful where there is anomaly of uterine action, postmaturity, slight ante-partum hæmorrhage, meconium staining of the liquor, toxæmia, malpresentation and minor disproportion.

In our Unit in Portsmouth, the charts are in fact used in all cases of labour, normal and abnormal, and I would recommend them on the grounds that they have helped to lower the stillbirth and neonatal death-rates.

Dr. C. N. Smyth (London) read a paper entitled *Uses of Fœtal Phonocardiography in the Labour Ward.*

Meeting
June 24, 1960

URINARY INCONTINENCE IN WOMEN

Professor N. C. Louros (Athens, Greece):

A Simple Operation for Stress Incontinence

[*Summary*]

The main idea which dominates all surgical procedures for the treatment of stress incontinence is to attempt to replace and fix the urethra and the neck of the bladder to their physiological condition.

Our method consists of fixing the vesico-uterine fold to the posterior wall of the uterus. By this procedure, the fundus of the bladder is pulled backwards, the urethra is straightened and its flexion corrected, re-establishing the normal relationship between the urethra and the bladder.

The first step is a Gilliam's ventrosuspension. The two round ligaments are drawn through the parietal peritoneum under the fascia of the rectus muscle and sutured by three silk stitches on either side, with the knots on the outer surface of the fascia. Thus, the uterus is placed upwards and forwards.

The second step is to draw upwards the vesico-uterine fold and to suture it on the lower part of the posterior surface of the uterus.

In the case of a rectocele and/or cystocele the operation is completed by an anterior and/or posterior colporrhaphy.

Thus, before operation a prolapse of the urethra and the neck of the bladder is noticed with an excessive alteration of the normal conditions but after the operation these organs are put into their normal position and the displacement of the bladder neck is corrected.

Urethrocystography is done before and after the operation. The bladder is filled with 100–150 c.c of collargol and in order to delineate the position of the urethra a fine chain is introduced through the urethra into the bladder. In the radiographs the edge of this chain represents the urethral os and the bladder neck.

Before operation radiographs show a marked descent of the fundus of the bladder indicated by the distance between the chain and the upper edge of the pubic os. This distance is approximately 4 cm constituting the unmistakable sign of the lowering of the urethra.

After operation, a notable shortening of this distance is evident, hardly reaching 1 cm. This elevation of the urethra by 3 cm constitutes in our opinion an unmistakable sign of the replacement of the urethra and the bladder in their normal positions.

Further proof is obtained by the length of the chain, which appears to be shorter in the pre-operative radiographs, due to the projection of the urethra, than in those taken after operation.

We have treated 126 women by this method, 96 (76·1%) are between 30 and 50 years old, living a normally active life, having a normal physical development and 94 of them a normal menstrual cycle, with a normal amount and duration of menstruation. In their obstetrical history, 1 to 9 either spontaneous (82·6%) or operative deliveries (17·4%) were reported.

All women complained of involuntary loss of urine (drop by drop) in a standing position after laughter, coughing or sneezing, i.e. after increasing intra-abdominal pressure. It is easily understood that incontinence is more marked in multiparæ than in primiparæ.

Gynæcological examination revealed in 64 cases a retroverted uterus accompanied by perineal laceration of 1st to 2nd degree. The adnexæ, parametriæ and the pouch of Douglas were free.

In a case with retroverted uterus a cyst of the right adnexa and a laceration of first degree co-existed. The left adnexa, parametrium and pouch of Douglas were normal. In 4 cases the uterus was retroverted, the adnexæ, parametriæ and the pouch of Douglas were free.

In 27 cases the uterus was also retroverted but besides a 2nd-degree perineal laceration a cystocele co-existed; the adnexæ, parametriæ and the pouch of Douglas were free.

In 28 cases the uterus was markedly retroverted, a cystocele co-existed, the perineum showed a laceration of 2nd degree and the pouch of Douglas a slight hernia. The adnexæ and parametriæ were normal.

Finally in 3 cases, besides the existing displacement of the uterus and a 3rd-degree perineal laceration, marked anterior and posterior cystoceles were present.

In this total of 126 women, in whom the above-mentioned operation was done, 58 had anterior-posterior colporrhaphy and 64 posterior colporrhaphy, and 4 ventrosuspension only.

All women were regularly followed up after the operation. 42 have been followed up for four years, 34 for about three years and 28 for eighteen months; these 104 women (82·5%), who

have been systematically re-examined, have not complained of any difficulty of micturition.

A second group of 9 women (7·2%) complained of unspecified vesical troubles, from one to six months after operation, without incontinence. Finally, 13 women (10·3%) showed no improvement at all after the operation.

Thus, by this surgical procedure a definite cure of incontinence can be expected in 82·5% of the cases. I believe that our method is highly efficient, and has the advantage of being simple and harmless.

(For fuller accounts of this operation *see:* LOUROS, N. C. (1958) *Rev. franç. Gynec.*, **53**, 411; LOUROS, N. C. (1959) *Zbl. Gynäk.*, **81**, 225.)

Mr. H. P. Winsbury-White (London):

Urethroscopy in Women with Incontinence of Urine

The most practical contribution I can make to this discussion is to emphasize that incontinence of urine often occurs with posterior urethral or bladder-neck irritations.

The most arresting examples of this group which come to my mind are not very common and are: (1) Diurnal incontinence of childhood. (2) Nocturnal enuresis commencing in adolescence, or young adults. (3) Daily incontinence which can be controlled by passing water frequently. This last state begins in childhood (often in infancy) when there is nocturnal enuresis, and the daily incontinence goes on into adult life, when there is also an occasional nocturnal enuresis. This last condition is mostly in single nulliparous women, for the very good reason that the patient shrinks from the embarrassment of married life. The urine is generally clear and sterile, and there is no residual urine in the bladder. This type of case undoubtedly provides most of the patients with stress incontinence in the nulliparous woman.

Clinically, in all these groups, there is a tendency to attacks of cystitis, or bouts of frequency of micturition. This often leads to urgency and incontinence. These are signs that the pathology is local, either in the posterior urethra or at the bladder neck.

The urethral mucosa.—The female urethra is lined by gland elements which resemble the tissue of the prostate. The glands are racemose in structure; once infection settles in them, it is difficult to eradicate. Indeed it lies latent, and flares up from time to time. Tonsillar glandular tissue is the same, and infection in this tends to behave in the same way.

Inflammatory characteristics are commonly seen with the urethroscope in many female urethræ, not only in incontinence but in others who suffer from disturbances of micturition; not the least important of these are those who suffer from attacks of cystitis, or chronic frequency of micturition.

Urethroscopic findings.—There are no urethroscopic characteristics which can be associated with special clinical features, so that incontinence is for the most part evidence of extreme urethral irritation, which may occur with variations of urethral pathology.

The best type of urethroscope is the Swift Joly, a modification of an older and equally excellent instrument, the Geiringer.

Urethral caruncle is of course at once seen and dealt with from the outside. It is the internal urinary meatus which is the commonest seat of inflammatory vegetation in women; when on the vesical aspect these are best seen and dealt with through the cystoscope (Figs. 1, 2 and 3).

FIG. 1.

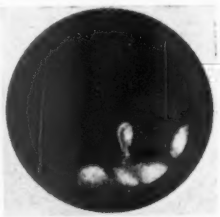

FIG. 2.

FIG. 1.—Part of the internal meatus viewed from the posterior urethra, showing early inflammatory projections (hillocks). When probed with the end of the urethroscope, these do not disappear.

FIG. 2.—Inflammatory polypus near the internal urinary meatus, view from the posterior urethra.

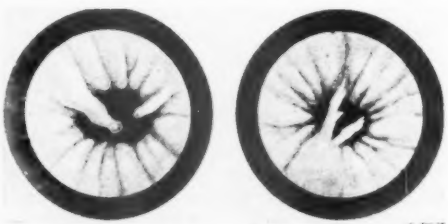

FIG. 3.—Polypi and mucosal folds seen together in the posterior urethra. The mucosal folds run longitudinally.

Broadly there are three types, polypi, granulomata and hillocks. It would be peculiar if inflammation of the internal urinary meatus did not also involve the adjacent trigone (urethrotrigonitis). Sometimes this vesical involvement is so localized on the trigone to the meatus that it can easily be missed with the cystoscope.

A perplexing feature of these cases is that the urine is often sterile in spite of urethroscopic findings. A special urethroscopic feature indicating inflammation is that the more simple vegetations tend to come and go. The vegetations represent two facts: (1) There is a focus of infection in the tissue, beneath each vegetation. (2) The focus drains poorly. These foci provide recurring manifestations of latent infection.

The necessary treatment is obviously to destroy the vegetations by coagulation through the operating urethroscope, and thus open up the underlying infective focus (Fig. 4). A general anæsthetic will be required, and the patient kept in bed for three days or so. The medical attendant should be warned that the patient is certain to be under the weather for about a month after the operation, during which time there may be an occasional attack of cystitis,

FIG. 4.—Pockets in the floor of the posterior urethra, opened up by coagulation of vegetations.

some frequency with terminal dysuria, or hæmaturia; but with copious fluids, and a short course of medication and rest, all symptoms should soon pass. Beware of the patient who on the first visit is obviously, from her deportment and speech, well under sedatives. Rest in bed with prolonged supervision will be necessary before surgical treatment will do any good, so that complete co-operation between physician, surgeon and medical attendant is essential. In my experience alcohol ultimately looms very largely in such a case.

Sometimes, after a vegetation has been clearly seen, it is no longer visible a month or so later. This leads to confusion amongst the inexpert in urethroscopy but calls attention to the fact that flimsy vegetation can disappear from mere simple instrumentation. Moreover the patient says that since the first examination there is an improvement in both general health and local symptoms. These are regular features with many patients and call attention to the benefits of a mere urethral dilatation—I would say by providing drainage from natural or adventitious openings in the urethral walls; however, these results can give a false impression of a complete cure. Sometimes a coagulation has to be done a second time, but urethroscopy decides this. I generally pass a sound three months after operation, especially if the urethra is narrow pre-operatively. Indeed it may be necessary to do several post-operative stretchings, at two to three months intervals. One should aim at keeping the urethral calibre at about 29 charrière.

Wyndham Powell straight anterior urethral male sounds (Fig. 5) are the only satisfactory

FIG. 5.—The Wyndham Powell straight urethral sound.

instruments for carrying out this work because they are finely graded; there is only one charrière between two adjacent sizes. Generally I use five successive sizes for each treatment, commencing with 23 or 24. The results of the combined coagulation and dilatation treatment are excellent. The consequences of carrying out the treatment unskilfully are well known. It takes two to three weeks for the urethra to settle after instrumentation. Too frequent dilatations are the common misuse of the treatment.

Residual urine and continued infection in the urine are important factors in deciding treatment, and call for caution.

Urethral contraction is fairly common, and is identified by noting the calibre of the urethra, by taking a size 24 Wyndham Powell sound. Size 26 charrière should lie comfortably in a normal female urethra, but in practice the test should not be made with this instrument. I always test the calibre with a size 24; if there is any gripping of this instrument there is undoubtedly urethral contraction.

When the trauma from parturition is remembered, it is not surprising that narrowing is frequently noted. The channel may suffer no more than a generalized bruising at confinement, and actual contraction may take years to develop. On the other hand it is occasionally congenital in origin.

The presence or absence of residual urine in the bladder is not a reliable guide to urethral narrowing. Contracted urethræ may be quite free from vegetations urethroscopically.

The internal meatus often gives a most interesting appearance when seen from the posterior urethra. Instead of seeing the uniformly crenated appearance due to the longitudinal folds of the urethral mucosa (Fig. 3)

of the internal meatus, this structure when seen from the posterior urethra is rigid and rounded, probably from fibrosis (Fig. 6). In Fig. 6 there

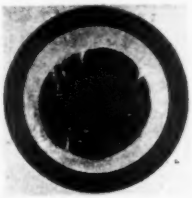

FIG. 6.—Urethroscopic view of the internal urinary meatus. Note the absence of mucosal folds. This is a fibrotic change. The flimsy tags are the type which disappear as a result of a single instrumentation (urethroscopy).

are fine polypoid tags, which would not be seen at a subsequent examination in a month or so. Such delicate fronds tend to disappear as a result of the original urethroscopy.

In other words to assess the importance of urethral contraction we must attune our minds to recognize different degrees of it, not in an extreme form. Anatomically there are four forms of it, involving respectively, the external meatus, the internal meatus, the whole passage, or any combination of these.

A simple meatotomy, with post-operative supervision, is often essential when the external meatus is involved.

All types of urethral contraction require an occasional urethral dilatation at proper intervals. It should be done with the instruments mentioned, at properly spaced intervals under local anæsthesia; to do it only once under a general anæsthetic with the wrong instrument is harmful and slipshod.

Intra- and extra-urethral causes of incontinence may occur together, and the urethra should be examined with this possibility in mind.

Whenever I find gynæcological causes I hand the case over to the gynæcologist.

Intra-urethral causes of incontinence are often present, and when found the proper treatment is highly satisfactory.

Young surgeons who are anxious to become proficient in urethroscopy should train themselves early. Facilities for training may not be easy to find. Patient and prolonged experience will be necessary. Ultimately they should be able to make this examination in the consulting room. Practically all females (except children), and probably all males under 50, can be urethroscoped this way.

Dr. D. W. Warrell (Sheffield):

Cystoscopy in the Investigation of Urinary Incontinence

Incontinence of urine may present a problem which cannot be solved by clinical examination. It can hardly be over-emphasized that the ætiology of urinary incontinence is complex, so that no single investigation can be expected to measure all the various factors which may be concerned with the loss of urinary control.

In the Department of Obstetrics and Gynæcology in the University of Sheffield all problem cases of urinary incontinence are carefully studied and investigated using radiology, cystometry, and cystoscopy. A case qualifies as a "problem" if there is incontinence without prolapse or if the patient has been referred because of operation failure.

Before discussing cystoscopy in the investigation of urinary incontinence I wish to make it clear that we believe if a case merits investigation then it should be investigated by all the techniques available, of which cystoscopy is only one.

In this series, 113 problem cases have been studied, and for comparison a control group of 24 cases of clinically straightforward stress incontinence due to bladder neck prolapse have been cystoscoped. The findings in these two groups are compared.

In the control group, 22 patients had normal cystoscopy findings, the other 2 showed a mild degree of urethro-trigonitis.

In contrast, 48 out of the 113 problem cases studied showed abnormal cystoscopic findings (Table I).

TABLE I.—CYSTOSCOPIC FINDINGS IN 113 CASES WITH URINARY INCONTINENCE

Urethro-trigonitis	14
Interstitial cystitis	16
Basal hæmorrhages	15
Avascular changes	6
Trabeculation	7
Distorted bladder base	2

16 were suffering from interstitial cystitis with findings of increased vascularity and mucosal change varying from exfoliation to atrophy and ulceration and 14 were diagnosed as suffering from urethro-trigonitis with cystoscopic findings of a vascular trigone with bullous œdema or a rough, red mucosa and a lumpy or frankly polypoid internal urethral meatus (Winsbury-White, 1956).

These two groups can be considered together for in both an inflammatory lesion causes bladder irritability. As might be expected, all these patients had frequency and urgency, in most cases amounting to urge incontinence. In addition, 24 of these 30 patients gave a history of incontinence on strain. In 11, the symptom of stress incontinence had overshadowed other

urinary symptoms and the patients had been referred because of operation failure.

The questions may now be considered: Why should patients with an irritable bladder leak urine on strain? How does a chronic inflammatory lesion of the bladder cause stress incontinence?

It is known that the detrusor muscle of the bladder and the involuntary urethral sphincter have a reciprocal action (Denny-Brown and Robertson, 1933) so that when the detrusor muscle contracts the involuntary urethral sphincter relaxes. In case of interstitial cystitis and urethro-trigonitis the detrusor muscle is constantly irritated and its tone raised. In these cases it seems reasonable to suppose that the urethra is reciprocally relaxed and its sphincteric power weakened so that when intravesical pressure is raised, for example by a cough, urine will escape via the relaxed urethral sphincter. Certainly these patients have small-capacity bladders with raised intravesical pressure indicating increased detrusor tone.

Support is given to this view by the results of treatment with urethral dilatation and silver nitrate instillations, for patients who respond are cured not only of their frequency and urgency but of stress incontinence as well.

The 15 patients with petechial hæmorrhages of the bladder base all had gross frequency of micturition. In 4 the finding was associated with urethro-trigonitis, in 2 with bladder neck obstruction, and in another 2 with gross urethral damage. In the remaining 7 there was no other lesion except mildly increased vascularity of the trigone, and in these 7 patients the gross urgency and frequency had been judged to be a neurotic or hysterical symptom.

I do not know if the finding of petechial hæmorrhages of the bladder base merely reflects disturbed bladder function in neurotic patients, or if it can be the cause of their symptoms.

6 cases showed avascular changes of the trigone and bladder neck. These were cases of post-radium fibrosis or of fibrosis following numerous operations on the bladder neck. The cystoscopy findings were not unexpected, but in these patients helped to confirm the clinical picture of a devitalized bladder neck embedded in fibrous tissue.

7 cases showed trabeculation. In 5 the detrusor muscle of the bladder had hypertrophied in an attempt to overcome bladder neck obstruction. In 2 it was the end-result of chronic urethro-trigonitis.

Lastly, 2 cases showed a grossly distorted bladder base, one following chronic pelvic sepsis and the other after operation. In these 2 cases cystoscopy was important, for the lesion was not recognized in any other way. Both recovered urinary control after the bladder base was freed by operation.

To summarize, cystoscopic changes were present in over one-third of the cases studied, compared with 2 out of 24 patients with straightforward stress incontinence.

Sometimes the cystoscopy findings were unexpected, more often they confirmed the results of other investigations.

The greatest use of cystoscopy was to distinguish the irritable bladder due to interstitial cystitis or urethro-trigonitis from the nervous bladder due to mental upset, and from the bladder with frequency due to the drag of a cystocele or the stretch receptors in the trigone.

Patients with urinary incontinence may give a clear-cut history and may have an obvious explanation for their symptoms—conversely these patients may require prolonged study and investigation and it is in this group that cystoscopy is most useful.

Acknowledgments.—I wish to acknowledge my gratitude to Professor C. S. Russell, who initiated this study, for his consistent patience, encouragement, and criticism; and to the Board of Governors of the United Sheffield Hospitals, who financed it.

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Dr. Göran Enhörning (Stockholm, Sweden):

Simultaneous Recording of Intra-urethral and Intravesical Pressure in Women [Abstract]

The pressure within different parts of the urethra can be recorded simultaneously with the intravesical pressure by means of a specially designed double-lumen catheter, two electromanometers and a recording apparatus. These pressures are measured when the patient is lying in the lithotomy position, when she is relaxing and when she is coughing vigorously.

With this method it has been found that normally a cough increases the pressure within the upper urethra simultaneously with the pressure within the bladder; both organs seem to be intra-abdominal. The intra-urethral pressure remains higher than the intravesical pressure even at the peak of a cough and urine cannot be expressed down through the urethra.

In cases of stress incontinence a cough increases the pressure within the bladder more than it increases the pressure within any part of the urethra. The difference between the highest

intra-urethral pressure and the intravesical pressure is zero or negative at the moment the incontinence is manifested.

The urethra will function satisfactorily as a closing mechanism if the pressure within its upper part is higher than the pressure within the bladder and if this upper part of the organ is above the pelvic floor. An increase of the intra-abdominal pressure will then reach the upper urethra to the same extent as it reaches the bladder, and the intra-urethral super-pressure will be preserved.

Mr. C. A. Simmons (London) read a paper entitled *Rapid Serial Urethrocystograms with Simultaneous Vesical Pressure Recordings.*

Dr. K. V. Bailey said that there existed a small percentage representing the worst cases of pure stress incontinence—which were dissociated from nervous conditions, trigonitis or other extraneous pathology, and in which the symptom was severe and the distress acute. 15% of those actually complaining of stress incontinence came into this group and could be recognized also from the type of cystogram they showed (Types B2 and C3). They were unlikely to be cured by a vaginal plastic operation alone, as sufficient elevation of the upper urethra with tissue contact at that site was not produced by this means. The Manchester colporrhaphy was a necessary phase in the operative treatment, but it must be combined with a procedure to secure this elevation and contact.

The combined colporrhaphy-fixation operation (Bailey (1954) *J. Obstet. Gynæc., Brit. Emp.*, **61**, 291; (1956) **63**, 663) was designed to produce this and to restore the anatomical status quo as nearly as possible with the traumatized tissues available. This operation was reserved for these worst cases. The Manchester colporrhaphy alone (or other plastic procedures) could adequately deal with the majority of cases, which were associated with lesser degrees of stress incontinence.

Operative results should cover a period of five years—and success should show both a clinical cure and an anatomical restoration of the upper urethra and bladder base to near normal.

The two-year results of the colporrhaphy-fixation operation showed 33 clinical and 29 anatomical cures in 35 cases and the five-year results showed 12 clinical and 11 anatomical cures in 14 cases. These satisfactory results show that: (1) Complete loss of the posterior urethrovesical angle combined in some cases with collapse of the upper urethra is the key anatomical factor in the production of stress incontinence, and (2) the reconstruction of the normal bladder neck anatomy—as far as this can be done—is the main factor in the production of a cure.

Mr. E. Schleyer-Saunders confirmed the good results of the operation described by Professor Louros against stress incontinence. He had used this technique for many years in all cases of suspension of the uterus, to add additional support. Some patients reported that they had lost the stress incontinence, or that it had greatly improved.

In stress incontinence combined with cystocele he had achieved the same results by fixing the bladder peritoneum to the fundus of the uterus on the vaginal route and plication of the vesicovaginal fascia underneath the trigonum.

He also confirmed that hormonal deficiency could cause urge incontinence. Œstrogen deficiency led to shrinkage of the fibrous tissue around the urethra, especially near the internal meatus, and transformed the urethra into a rigid canal. In consequence, the mucosa of the urethra was put into folds which acted in the same way as inflammatory granulations or polypi. Œstrogen softened the fibrous tissue and restored the urethra to normal shape. It also increased the tonus of the bladder muscles.

He had used œstradiol implants in 500 menopausal women during the last fifteen years, and many of them who complained of urge incontinence were cured after the implants. Dilatation of the urethra as recommended by Mr. Winsbury-White could also help.

Professor J. Chassar Moir said the essential point about Professor Louros's operation was the elevation of the bladder as a whole to a higher level. Whereas in the well-known Marshall-Marchetti operation it was the *anterior* wall of the bladder which, together with the urethra, was raised and attached to the back of the pubes and the recti muscles, in the present operation it was the *posterior* wall of the bladder which was raised and attached to the fundus and body of the uterus. The effect of this must be similar to that of the old "interposition" operation which was primarily performed for prolapse but which also cured many cases of stress incontinence. In both operations the bladder was made to rest "piggy back" on top of the uterus.

Professor J. C. McClure Brown said that apparently opposite points of view had been presented.

Professor Louros cured stress incontinence by elevating the bladder to straighten the posterior urethrovesical angle, but many would believe, with Roberts, Jeffcoate and Malpas, that the way to cure stress incontinence was to *increase* the posterior urethrovesical angle.

These opposing points of view can be reconciled. The key to the situation was the simultaneous rise in pressure in the upper urethra and in the bladder, when the former was an intra-abdominal structure. Probably what is done when we cure stress incontinence is to elevate the bladder base and upper urethra so that these are returned to the abdominal cavity where they properly belong.

Mr. Winsbury-White's contribution on urethroscopy, and Dr. Warrell's observations on cystoscopy had served to remind us that many of the problem cases of so-called stress incontinence are in fact the result of lesions in the bladder neck and upper urethra—a fact which gynæcologists tend to overlook.

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Meeting
June 23, 1960

Reduction in Colonic Mucosal Absorption with Reference to the Chemical Imbalance of Ureterocolostomy

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Introduction

Improvements in technique, together with sulphonamides and antibiotics, have made ureterocolostomy a progressively less formidable procedure from the standpoint of immediate post-operative mortality. Now the late complications of renal damage and electrolyte imbalance are being more closely studied.

Renal damage has long been known to be a serious complication of ureterocolostomy patients and the clinical evidence of this has been reviewed elsewhere (Irvine *et al.*, 1956).

The high incidence of electrolyte imbalance has only recently been recognized. In a series of experimental studies previously recorded (Irvine *et al.*, 1956) evidence was presented that the primary cause of the imbalance was absorption of the urinary constituents across the colon mucosa though renal damage might be expected to increase the biochemical disturbance.

If ionic absorption across the colon mucosa is the important primary factor in chemical imbalance it would seem worth while to investigate means of inhibiting this process. Indeed, in some patients after ureterocolostomy a spontaneous reduction in ion transport into the blood stream and in the differential excess of chloride reabsorption over sodium has been noted to occur (Care *et al.*, 1957). Intraluminal irradiation was well known to reduce the secretory activity of the gastric mucosa (Ivy *et al.*, 1923; Palmer and Templeton, 1939; McKendry, 1950; McGeorge, 1950; Simon, 1949; Douglas *et al.*, 1950). Since the colon mucosa was known to be more sensitive to irradiation than the stomach (Regaud *et al.*, 1912; Lawrence and Tennant, 1937; Warren and Friedman, 1942), and the absorptive surface less deeply placed than the parietal cells, it was considered possible that colonic mucosal absorption might also be reduced by this means. Although much information was available on the histological appearances of the colon after irradiation (Bloom, 1948), the effect on its function of absorption was not known.

The aim of the present experiments was to study the absorption of chloride and sodium from colon loops and pouches before and after irradiation. Since it was hoped to reduce mucosal activity without interfering with motility, it seemed desirable to use intraluminal irradiation employing a beta-ray-emitting material which, having a low penetration, would affect mainly the mucosa. What was wanted was a radiocolloid of short half-life and high specific activity emitting energetic beta rays only and remaining essentially completely in the colon. Yttrium 90, with a half-life of sixty-six hours, and a maximum beta-energy of 2·24 MeV, was found to meet these requirements and was therefore used in these studies.

Since such intraluminal irradiation might interfere with colon motor activity, this was also measured in some of the absorption experiments by methods described elsewhere (Irvine *et al.*, 1961).

Experimental Plan and Materials

Using the radioisotope methods described below, the absorption of isotonic saline from canine colon before and after irradiation was studied in two groups of dogs. In the first group (9 dogs) a loop of lower colon was used with black silk serosal sutures to define its limits. The bowel was exposed on each occasion by open operation and each experiment was carried out under general anæsthesia. In the second group (4 dogs) an isolated colon pouch was prepared under strict aseptic conditions. This allowed repeated studies to be made under general anæsthesia without reopening the abdomen. Both animal preparations are illustrated in Fig. 1.

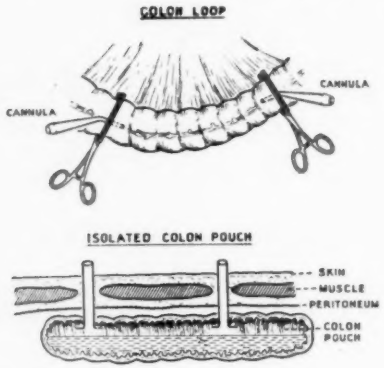

FIG. 1. — Diagrammatic representation showing method of isolating colon loop and anatomical arrangement in isolated colon pouches.

Isotope materials.—Radioactive chlorine 36 and sodium 24 were obtained from the Radiochemical Centre, Amersham. ^{24}Na (half-life fifteen hours, maximum gamma-ray energy 2·76 MeV, maximum beta-ray energy 1·39 MeV) was supplied as isotonic saline. ^{36}Cl (half-life $3{\cdot}1 \times 10^5$ years, maximum beta-ray energy 0·714 MeV) was delivered as 2N HCl, which was neutralized with sodium bicarbonate and made isotonic prior to use.

The yttrium preparation consisted of colloidal yttrium stabilized with dextran and irradiated with neutrons in a reactor. It was chosen after experiments had clearly indicated that it was not absorbed through the colon mucosa. It was specially prepared for this work by the staff of A.E.R.E., Harwell. Its main disadvantage, which will be further mentioned, was that it was strongly hypertonic.

Absorption methods.—Three tracer methods were used. In the first the rate of fall in ^{24}Na concentration in the isolated pouch was measured directly by means of a gamma-sensitive G-24Pb Geiger-Müller counter (20th Century Electronics) mounted over the pouch or loop containing the ^{24}Na solution; quantities of 100 μc were used for this purpose. The output from the Geiger-Müller tube was fed to an Ekco ratemeter type N.522A via a probe unit type 1014B and the fall in activity was recorded graphically against time on the recording ammeter (Evershed and Vignoles) linked in parallel with the ratemeter. By this means it was easy to observe the rate of removal of radioactivity from the colon lumen continuously throughout the experiment.

It was impossible to study chlorine transport by this method since the isotope used, which is the only feasible one, emits only beta rays.

A second source of information concerning ^{24}Na transport and also that of ^{36}Cl was obtained by aspiration of the lumen contents at the end of the absorption period. When measurements of ^{36}Cl transport were being carried out in this way 5 μc of ^{36}Cl was added to the experimental solution used in the colon. Several washings were normally required in order quantitatively to remove all radioactivity from the lumen. These were all pooled, the aspirate becoming diluted in the process to a volume of approximately 100 ml, this total volume being used for radioactive estimation of the contained ^{24}Na. The gamma-ray emission of an aliquot of the aspirate was measured by placing it in the centre of a ring of eight gamma-sensitive G.24Pb Geiger-Müller tubes connected in parallel. The count rate obtained from this aliquot was then compared with that of a standard prepared from a known volume of the original solution which had been retained before the experiment began. In this way the percentage of ^{24}Na remaining in the aspirate could be determined.

Thirdly, further measurements, made on the aliquot and standard after decay of ^{24}Na, could also be used for determination of the contained ^{36}Cl. For this purpose a beta-sensitive liquid counter type M.6 (20th Century Electronics) was used; and in practice it was usual to delay this measurement for fourteen days.

Technique of absorption studies.—The capacity of the surgically prepared loop or pouch was measured by determining the volume of physiological saline able to enter to a pressure of 5 cm saline. Absorption experiments were conducted after washing out the pouch or loop by instilling labelled physiological saline, the volume being equal to half of this measured capacity, which gave comfortable filling without distension, the hydrostatic pressure varying between 0·5 and 1·5 cm of saline.

In the loop preparations labelled isotonic saline was instilled via a cannula, the marked length of colon being temporarily isolated with non-crushing clamps. During the period of absorption the bowel and clamps were returned to the abdominal cavity. After an interval of 30 minutes, when approximately 50% of the sodium and chloride had been absorbed, the loop was completely aspirated, and the volume recorded. In many cases half of this initial aspirate was kept for chemical analysis. The loop was then irrigated three to four times with 20 ml of isotonic saline, the total aspirate being retained for subsequent determination of activity. The abdomen was then closed and each subsequent experiment in absorption required a further laparotomy. The same technique was followed each time, care being

taken to apply the clamps exactly opposite the marker sutures.

In the pouch preparations, after irrigation to remove mucus and instillation of the isotopes, a gamma-sensitive shielded G.24Pb counter was placed directly over the pouch, in contact with the surface of the abdomen, and the disappearance of activity recorded, as described, over thirty minutes. At the end of this period the pouch was aspirated and irrigated with isotonic saline to remove any remaining radioactive material; counting was then carried out as with the loops.

Control study with double colon loops.—In order to determine whether radioactive ions entering the blood stream and passing back into the colon loop contributed materially to the radioactivity remaining at the end of the 30-minute period, dogs were prepared with two separate colon pouches; into one was instilled isotope-labelled physiological saline and into the other ordinary physiological saline, under identical conditions. At the end of the 30-minute period the fall in radioactivity in the colon pouch with isotope-labelled saline was found to be associated with just detectable activity in the other. This activity accounted for less than 1% of the radioactive material in the pouch which had contained labelled ions. It was therefore concluded that reduction in isotope activity in the contents of the colon loops measured mainly unidirectional movement of labelled ions from the colon lumen into the blood stream.

Control studies using chemical and isotopic measurements of sodium and chloride.—In 3 of the dogs in this group chemical estimations of sodium and chloride were made from an aliquot of the removed fluid at the end of the absorption period.

Chemical methods.—Sodium was measured by the flame photometer and chloride by the Volhard-Harvey method (*see* Harvey, 1910).

These results made it clear that the measurement of disappearance of labelled ions from the colon lumen was not attended by the passage of unlabelled ions in the opposite direction to any marked extent. In short, the isotopic measurements of ions transport were essentially net absorption results.

Irradiation Methods Using Intact Colon Loops

(1) *Direct instillation of radioactive yttrium* 90.—The intact loop was prepared and cannulated as for an absorption experiment. Colloidal yttrium 90 was directly instilled until the loop was evenly distended. A statement of the activity of the preparation when leaving Harwell was supplied and, through knowledge of the half-life, the activity at the time of instillation could be calculated as described later, and from that the dose delivered to the mucosal surface in a finite time and at known volume.

The time required to give a specific dose was thus calculated and at the end of this period the active material was aspirated from the loop and the bowel irrigated to remove residual yttrium.

There were disadvantages to this technique. The yttrium 90 colloid was strongly hypertonic, which caused the fluid contained in the lumen of the bowel to increase in volume, thus diluting the irradiating solution. Despite this, the dose delivered could be subsequently calculated through measurement of the degree of dilution; but where this was appreciable the dose did not correspond with what had been planned. A further and more serious disadvantage was that the strongly hypertonic material often irritated the bowel and caused an increased secretion of mucus which, when present in quantity, reduced the effect of the irradiation in a manner which was quite indeterminable.

However, this was the only method which could be used for the isolated colon pouches.

(2) *Irradiation via an intraluminal balloon.*—A thin-walled cylindrical rubber balloon was constructed which, on distension, completely filled the colon loop, the mucosa lying in close and even apposition. The balloon was mounted on a central firm rubber tube, introduced via the anus, and manipulated into position at open operation. The balloon was filled with active material through a fine side channel, the dead space being reduced to just over 1 ml.

This method avoids the problems of dilution and mucus secretion, but a correction for beta-ray absorption by the balloon wall was necessary when calculating the dosage delivered.

(3) *Dosage calculations* are described elsewhere (Irvine *et al.*, 1961).

Histological Methods

After the final absorption study each dog was sacrificed, the colon loop or pouch removed for gross examination and then segments removed from the irradiated area and the untreated colon for histological study. Fixation was by 10% formalin and sections were stained by hæmatoxylin and eosin and cut 7 μ thick.

Results

The results can be considered in three separate groupings: first, the initial pilot studies in 4 dogs with loop preparations, where a high dose of irradiation proved that absorption could be reduced, but with resulting macroscopic damage to the colon and abnormal motility patterns. In the second group of loop studies smaller radiation

doses were used which again reduced absorption, without serious colon damage histologically and no evidence of impairment in motor activity. In the third group are the dogs with isolated colon pouches, allowing many more absorption studies to be made. These studies again confirmed inhibition of absorption without gross morphological damage.

Group I.—Heavily Irradiated Colon Loops

There were 4 dogs in this group. An initially high dose of irradiation (1,930–3,104 rads) was chosen to determine at the outset whether mucosal irradiation affected absorption to any significant extent. Base-line pre-irradiation absorption studies were restricted to two or three readings only and were repeated on only two occasions some three months after irradiation. At this time gross pathological changes were present in 3 of the 4 dogs, which were then sacrificed. In the fourth, since damage appeared minimal, studies were repeated after a further three months had elapsed. The results obtained are illustrated in Fig. 2.

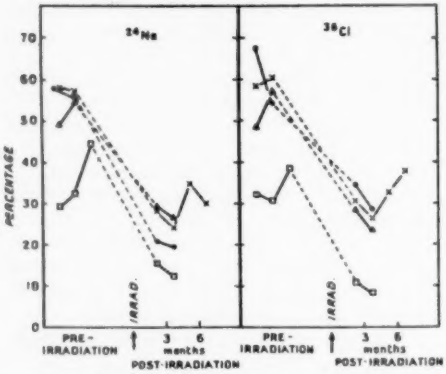

FIG. 2 (Group I).—Reduction in activity in colon lumen 30 minutes after instillation. Dosage to colon loop 2,000 to 3,000 r.

Pre-irradiation readings.—Absorption rates for both labelled ions were relatively constant in the individual animal and the standard deviations were small. However, there is variation in the absorption rates between one animal and another. In this group there is no statistically significant difference in the absorption of chlorine as compared with sodium.

Post-irradiation readings.—Three months after irradiation the absorption rates for both ions are approximately halved. The effect is not specific, both sodium and chlorine absorption being similarly reduced. The number of readings in the individual animals is too few for statistical analysis; but when they are considered as a group the reduction in absorption for both ions is separately significant, the probability being less than 0·5. In the one animal studied for six months there is a slight return towards pre-irradiation levels, but the reduction in absorption is still statistically significant.

Pathological findings.—Three of the four loops showed gross thickening of the wall of the colon loop and in two this thickening had produced some degree of stricture. Ulceration of the mucosa was frequently present. Histologically, the loss of colon epithelium with epithelial remnants regenerating, round cell infiltration of the submucosa and vasculitis were often seen (Fig. 3). Several dogs showed grossly abnormal motility patterns in this group.

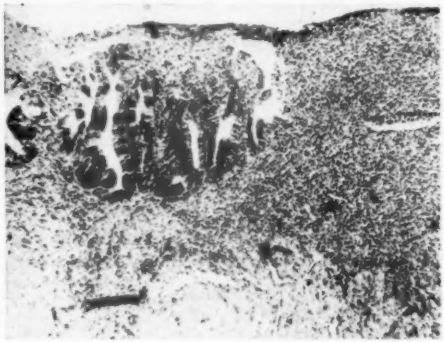

FIG. 3.—Effect of high dosage of irradiation on mucosa of colon loop.

Group II.—Colon Loops Receiving a Low Dose of Irradiation

The dose of irradiation was reduced to 750–1,220 rads in an attempt to reduce the injury to the bowel apparent in Group I. In all cases examination of the colon at three and six months after irradiation showed no significant macroscopical change in the irradiated segment. With one exception, all animals were studied for six months and at each period of the experiment a larger number of absorption readings was taken than in the first group. Fig. 4 shows the results.

Pre-irradiation readings.—Absorption rates for both ions in the individual animals are fairly constant and the standard deviations are smaller than in Group I. Again, there is quite wide variation in rate of electrolyte absorption between one animal and another. Taking this group as a whole, there is a greater absorption of chloride as compared with sodium, and this is statistically significant ($P<0·1$).

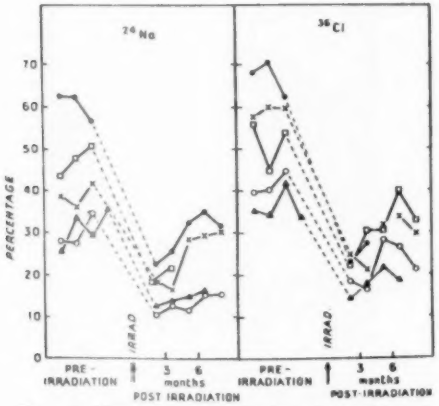

FIG. 4 (Group II).—Reduction in activity in colon lumen 30 minutes after instillation. Dosage to colon loop 750 to 1,220 rads.

Three-month post-irradiation readings.—Following irradiation, reductions in the rate of absorption for both ions are separately significant ($P < 0.5$) and in general the rates are 50% to 70% below the pre-irradiation levels. Despite the reduced dose of irradiation in this group, the effects on electrolyte absorption are no less marked than those seen in the heavily irradiated animals. The effect of irradiation is not specific, chloride and sodium absorption being similarly affected. The pattern of a slightly greater absorption of chloride as opposed to sodium, noted in the pre-irradiation readings, still persists after irradiation and is shown by all animals in the group.

Six-month post-irradiation readings.—In all animals there is a slight tendency for the absorption rates for both ions to increase towards their pre-irradiation levels, but at six months the reduced rates of absorption are still highly significant.

Pathological changes.—Macroscopically the 4 irradiated loops appeared normal. On inspection of the serosa, and when the loops were removed and opened, the mucosal surfaces showed no evidence of ulceration and the thickness of the bowel wall appeared normal. Microscopic examination revealed no gross abnormality (Fig. 5). The height of the epithelial cells may have been slightly reduced in one dog and in another a small area of submucosal fibrosis was seen. There were no abnormal mitoses.

Motility patterns were not altered by this dose of irradiation.

Group III.—Isolated Colon Pouches

There were 4 dogs in this group, two irradiated with 1,300 and two with 500 rads. The experimental data obtained in the isolated colon pouches are graphically recorded in Fig. 6.

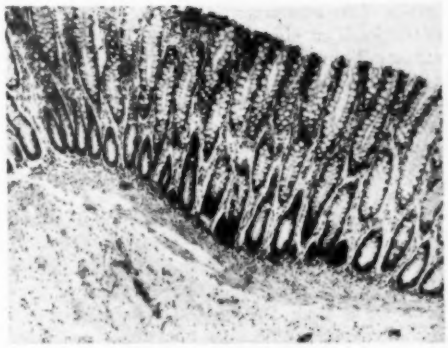

FIG. 5.—Effect of low dosage of irradiation on mucosa of colon loop.

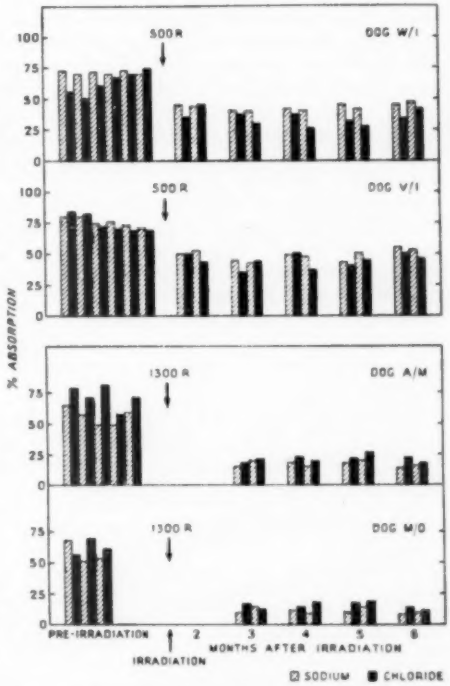

FIG. 6 (Group III).—Reduction in radioisotope activity in pouch lumen after 30 minutes.

Irradiation with 1,300 *rads.*—There is little individual variation between the two animals, but both show slightly greater absorption rates for chloride than sodium in the pre-irradiation period, and this is maintained throughout the

course of the experiment. Following irradiation, both pouches show a marked and sustained reduction in electrolyte absorption. This is apparent at three months and remains unchanged during the six months' experimental period. The effect is most marked in the second pouch, Dog M/O, where the fall in absorption rates for both ions is 70% to 80% below pre-irradiation levels. The fall in absorption rates for each ion is separately significant ($P<0{\cdot}1$). As in the intact colon loops, the effects are non-specific and both sodium and chloride absorption show proportional reductions. Both pouches show some evidence of slight histological damage and there is some reduction in pouch volume.

Irradiation with 500 *rads.*—Pre-irradiation absorption levels are similar in both animals. In contrast to the first two pouches, sodium absorption tends to run at a higher level than chloride. During the experiment the maximum effect on electrolyte absorption is apparent three months after irradiation, when the levels for both ions are approximately 40% below pre-irradiation readings. At six months there is a definite tendency to recovery in absorption rates, but this is slight and the reductions affected are still separately significant for each ion ($P<0{\cdot}1$).

The disappearance of labelled sodium as indicated by surface counting when plotted on semi-logarithmic paper against time produced a straight line which could be extrapolated to the theoretical time required for activity to be reduced 50%, assuming that the rate of absorption remained constant. This time interval significantly increased ($P<0{\cdot}01$) in each pouch after irradiation (Fig. 7).

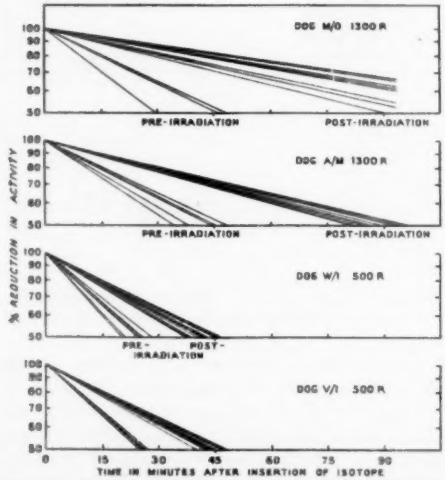

FIG. 7.—Results of surface counting of ^{24}Na activity in four pouches.

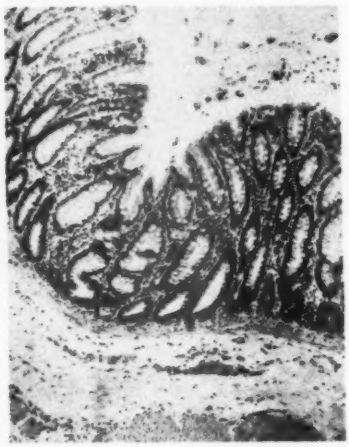

FIG. 8.—Effect of irradiation of mucosa on isolated colon pouch.

Pathological findings.—The pouches appeared macroscopically normal and histologically the walls of the pouches appeared normal. Fig. 8 represents the typical microscopic findings.

COMMENT

The isotope absorption studies reported here record mainly unidirectional movement of sodium and chloride ions from colon lumen to blood since experiments with double pouches showed clearly that less than 0·3% of the activity present in the lumen at the end of a half-hour period could be accounted for by backward movement of labelled ions into the colon lumen. The tests combining chemical and isotopic methods gave almost identical results in both pre- and post-irradiation states, allowing the conclusion that under the conditions of this study the unidirectional measurements closely approximated to the net absorption rate. Since pouch and loop volumes remained much the same before and after irradiation, especially in Groups II and III, comparisons of absorption rates before and after irradiation could be made.

In Groups II and III absorption rates were surprisingly constant for any individual animal, but there were wide variations within each group. Taking the pre-irradiation absorption results of each group as a whole, chloride appeared to be absorbed in excess of sodium in Groups II and III. In Group I there were fewer observations available for analysis and individual variations were much greater, perhaps because of imperfect techniques; but even in this group the overall picture is one of slightly greater chloride absorption, though it is not statistically significant. Larger periods of absorption may well have en-

hanced the difference between the amounts of chloride and sodium absorbed and in the ureterocolostomy patients many hours are available between voiding for reabsorption of the urinary constituents.

Intraluminal irradiation reduces significantly and equally the unidirectional movement of both sodium and chloride ions from colon to blood. At the higher doses of irradiation this is accompanied by gross morphological damage and evidence of motor dysfunction. At lower dosage this reduction of absorption can be produced without any evidence of histological damage and motor activity, as evidenced by the response to Prostigmin, appears the same. These studies suggest that it might be profitable to study experimentally the effect of intraluminal irradiation on the acidosis of ureteral transplantation. One possible side-effect of such treatment might be the effect of irradiation on potassium transport across the colon mucosa. Many ureterocolostomy patients are hypokalæmic and any increased loss of potassium would be serious. Such studies are at present in progress.

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Implantation of the Ureters into an Isolated Rectosigmoid Bladder

By L. N. PYRAH, M.Sc., Ch.M., F.R.C.S.

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PRIOR to 1950 the cause of the clinical failure, because of electrolyte imbalance, of some operations for ureterocolic anastomosis was not understood. In that year Ferris and Odel (1950) showed that hyperchloræmic acidosis develops following ureterocolic anastomosis in 75% of cases, but that in the majority of that 75% no clinical symptoms develop. A proportion of cases, a fifth to a quarter, however, do have symptoms of nausea, loss of appetite and a lack of the sense of well-being, and a still smaller proportion run into more dangerous symptoms, such as loss of weight, vomiting and sometimes coma and death. At first it was not understood how to deal with this chain of symptoms, which resulted partly from ascending renal infection from the colon to the kidneys and partly from the differential absorption of electrolytes from the colon, the acid chloride ions being absorbed in greater proportion than the basic sodium ions (Lapides, 1951; Parsons, Powell and Pyrah, 1952; Parsons, Pyrah, Powell, Reed and Spiers, 1952).

The disadvantages of ureterocolic anastomosis led to a search for alternative methods of urinary diversion, and the two principal ones which have been practised and advocated have been ileal ureterostomy, advocated first by Bricker (1950; Bricker *et al.*, 1954) and by Wells (1953, 1956), and the rectosigmoid bladder which I have advocated (Pyrah, 1956, 1957). The principle of these two operations is that the urine is deviated into a loop of intestine which is free from fæces, so that ascending renal infection is minimized.

The Rectosigmoid Bladder

In 1956 I reported to the British Association of Urological Surgeons 11 cases of rectosigmoid bladder with cystectomy (Pyrah, 1956) and the purpose of this communication is to bring the series up to date and to give the results. The procedure was first carried out by Mauclaire in 1895, but it was discarded.

Operation.—The operation has usually been carried out in two stages. The bowel is prepared by the administration of Aureomycin given orally. In the first stage, the sigmoid colon is divided transversely a little distance above the middle of the sigmoid loop, and the mesosigmoid including the marginal artery is divided at the line of section of the gut sufficiently deeply to allow the proximal end of the divided colon to be brought to the surface of the abdomen in the left iliac fossa without tension as an end-colostomy. The distal end of the sigmoid loop is infolded by two rows of catgut sutures. The new bladder then consists of the rectum and the lower half of the sigmoid colon. The left ureter is exposed and isolated at the outer side of the mesosigmoid

at the level of the brim of the pelvis, ligatured low down and divided; to avoid kinking it is usually transposed through a small opening in the base of the mesosigmoid to its inner side and is then anastomosed to the upper part of the recto-sigmoid. The method of the anastomosis of the ureter to the gut in nearly every case has been that of Cordonnier (1950) which employs a direct mucosa-to-mucosa technique. A period of ten to fourteen days is allowed to elapse to ensure the adequate functioning of the ureterosigmoid anastomosis. The bladder is then removed and the right ureter is anastomosed in a similar way to the rectosigmoid some distance below the left. The patient micturates *per anum*, and defæcation is via the colostomy.

Advantages of the operation.—(1) The operation is easy to perform in two stages which makes for safety. There is no intestinal anastomosis, as there is in the operation of ileal ureterostomy so that the operative risk is reduced. The post-operative course has been satisfactory and the incidence of ileus has been low.

(2) The artificial bladder, which has a capacity of between 400 and 500 ml, seems to empty satisfactorily and is not associated with undue frequency of micturition. The normal tone of the anal sphincter ensures continence and only in one case has there been slight occasional nocturnal incontinence.

(3) The new bladder does not contain fæces and seems to have a low bacterial content. The incidence of late ascending renal infection has been very low. The Cordonnier type of anastomosis is safe in these cases because of the reduced danger of ascending infection, and it is advantageous because the wide stoma permits free renal drainage and there is little tendency to late hydronephrosis or anastomotic stricture.

(4) Although we know from experimental results that differential absorption of chloride over sodium does take place even in this relatively short length of large gut (Pyrah *et al.*, 1955) yet, since the kidneys do not become infected, electrolyte imbalance is very unusual, though it occurs occasionally. Most patients do not need to take alkalis. We have also shown that in the length of gut used, the amount of differential electrolyte absorption does diminish with time (Care *et al.*, 1957).

(5) The colostomy is not a disadvantage. If there is to be urinary diversion other than ureterocolic anastomosis, the surgeon must choose between a urinary fistula (ileal ureterostomy) and a fæcal fistula (colostomy). I believe that in terms of post-operative morbidity and operative mortality the rectosigmoid operation is to be preferred to ileal ureterostomy (Wells, 1956).

(6) If the patient later objects to a colostomy, it can be re-converted to a formal ureterocolic anastomosis without disturbing the site of the anastomoses.

Results.—I have carried out the operation of rectosigmoid bladder with total cystectomy on 26 patients. There have been three post-operative deaths, one of which occurred three months after the operation from fistula and peritonitis, one from pulmonary embolism seven days after operation, and another from bronchopneumonia also seven days after operation. In my hands this mode of cystectomy has been a safer procedure than the one-stage cystectomy with ureterocolic anastomosis and several of the patients who have been too ill for ureterocolic anastomosis to be contemplated with equanimity have survived. Of the survivors, 8 died from metastatic cancer in periods varying from four months to five and a half years. 12 patients are alive and well from six months to eight years after operation.

Late follow-up.—In many of the earlier cases, intravenous pyelograms taken some months after operation showed perfectly normal kidneys. In the series as a whole examination of the renal status of 39 renal units, where post-operative X-rays are available, shows no hydronephrosis in 30, slight hydronephrosis in 7 and moderate hydronephrosis in 2. The fact that practically all of those with hydronephrosis show only slight hydronephrotic changes has made the results of this kind of transplant in my hands much better than transplantation of the ureters into the intact colon.

Ascending infection as a clinical complication has been limited to only 3 cases. Although we have shown that from the rectosigmoid bladder chloride in excess of sodium is absorbed into the blood stream yet, because of the relative absence of ascending infection, hyperchloræmic acidosis is very rarely a problem. Of the 26 cases, electrolyte imbalance was noted in only 4 patients; 1 of these had had a temporary urinary fistula which explained the renal infection and the corresponding kidney later became hydronephrotic. This small incidence of electrolyte imbalance is vastly different from the high incidence of imbalance when the ureters are anastomosed to the intact colon. In all the other 22 cases there was no sign of electrolyte imbalance.

All these patients, however, who have recovered from their operation, provided their malignant disease has not recurred, have enjoyed a very high grade of health. They have looked well, have had good appetites and have been normally active and mobile. We have not had, as we have had with the cases with a ureterocolic anastomosis, a fifth or so who have indifferent health, a grey look, and periods of loss of appetite and

inability to work their normal quota. The colostomy has not been complained of by the rectosigmoid patients.

Present position of case selection for the rectosigmoid bladder operation.—(1) If a patient has multiple vesical growths of low malignancy which require cystectomy, and if he is expected to live for a long time, ileal ureterostomy and the rectosigmoid bladder are the modes of urinary diversion of choice; of the two I favour the rectosigmoid bladder.

(2) We have become more confident in the biochemical and overall management of cases with ureterocolic anastomosis than we were between 1951 and 1955 (when I did several rectosigmoid bladders) and there has not been in the last few years quite the same pressure to get away from ureterocolic anastomosis as there then was.

(3) There is a small group of patients for whom the rectosigmoid bladder is the ideal procedure. Recently I have operated on 4 elderly men with bladder cancer, in whom one kidney was either completely or almost completely out of action from obstruction by growth, and in whom the other kidney showed early or moderate hydronephrosis. The blood urea was between 60 and 75 mg/100 ml. In such cases external radiotherapy may not give a sufficiently rapid improvement in the growth to preserve the function of the remaining relatively healthy kidney. A formal ureterocolic anastomosis in this group would run the risk of a higher than average mortality from renal failure, while a one-stage ileal ureterostomy would court a high mortality. The rectosigmoid bladder operation done in two stages has seemed to me to be easily the safest procedure, and these 4 patients survived.

Acknowledgment.—The author wishes to acknowledge with thanks the help and co-operation of Dr. Gretta M. Thomas in the follow-up of cases.

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Colocystoplasty

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THE indications for enlarging the bladder are well known and I will not repeat them. My object is to discuss the merits of a colonic as opposed to an ileal graft for the purpose.

The results of ileocystoplasty.—Since Couvelaire (1950) introduced the operation of ileocystoplasty into France several series of cases have been reported. Cibert (1957) reported 105 personal cases; Wells (1956) collected 55 cases from members of the British Association of Urological Surgeons, and Jacobs (1960) has recently reported on 28 cases. Whilst the results in most cases have been excellent the mortality and morbidity have been high, largely owing to the complications of ileus or intestinal obstruction following the small gut anastomosis. Wells (1956) reported 42 cases of ileus and 10 of mechanical obstruction in 207 patients who underwent uretero-ileostomy; of 55 who had ileocystoplasty 4 developed intestinal obstruction. This operation may be difficult in a stout patient who has been fattened up by sanatorium treatment and has a short mesentery. The variability of the results with the ileum and the evidence produced by Grégoir (1958) in favour of the colon made me decide to use the sigmoid colon instead of the ileum in a series of cases where bladder enlargement or substitution was needed.

Advantages of the colon.—There are many advantages in using the sigmoid colon rather than the ileum. It lies close to the bladder, it is easily mobilized and it usually has a redundant loop which can be readily spared. Its mesentery has a low origin and the whole procedure can be kept within the pelvis without disturbing the upper abdomen. It has a wider lumen than the small intestine which ensures a greater increase in bladder capacity and is a safeguard against stenosis of the restored colon after end-to-end anastomosis; a rectal tube can be passed up beyond the anastomosis to relieve distension and there is little chance of ileus. Its blood supply from the sigmoid arteries and their marginal arcades is abundant and the rectal surgeons have shown us that even after high ligation of the

inferior mesenteric artery a safe anastomosis is possible. Functionally it is more adapted to the process of expulsion and this should and does result in a more powerful urinary stream and less residual urine. Morales and his colleagues (1958) have suggested that as the centres for micturition and defæcation are both in the sacral part of the spinal cord the two functions have identical reflex mechanisms.

The former objection that it was more septic than the ileum is no longer valid as it can be sterilized easily.

Contraindications to the use of the colon.—The possibility of electrolyte absorption would seriously mar the procedure. Experimental work on dogs showed that it did not occur, nor has it been recorded in any of the published series in man. In the absence of bladder neck obstruction, which must be verified before operation, absorption is unlikely to happen when only the dome of the bladder is replaced. Even when the whole posterior wall and dome have been replaced by colon we have found no biochemical disturbance and it was present in only one patient with advanced pyelonephritis as a terminal event.

Local inflammatory disease occurs more often in the colon than the ileum and extensive diverticulitis or pericolitis would preclude its use although it has been used when there was mild diverticulosis. The presence of a new growth or previous resection for growth or diverticulitis would be obvious contraindications. An air enema before operation will indicate both its length and mobility and will exclude gross disease. Excessive fat makes the operation more difficult, as it does in ileocystoplasty. Previous radiotherapy reduces the chances of success, but we have used the procedure in 3 cases of extensive radionecrosis of the bladder with varying success.

Pre-operative preparation.—The usual method of emptying and sterilizing the colon is based on a low residue diet, colonic lavage, enemata and neomycin 1 g twice daily for two days. A bowel swab taken at operation is often sterile, or shows monilia, or only non-pathogenic bacteria.

Operative technique.—I am greatly impressed by the value of the open flap method which incorporates the graft into the bladder rather than the closed loop which leaves it as a diverticulum, even if it is isoperistaltic. Micturition is more forcible and less likely to be in two parts. There is no stoma to contract and much less trouble from mucus which in any event tends to get less as time goes on. I have used the closed loop in only 2 cases.

Moreover the final result looks more like a bladder although its mucosa remains columnar.

A rectal tube and a No. 22 (F) whistle-tip plastic urethral catheter are inserted before operation. The sigmoid colon is mobilized and a length of up to 20 cm chosen which will reach the bladder without tension. In dividing the mesentery at right angles to the bowel the transverse vessels are ligated individually with fine silk or thread. Oblique division of the bowel with excision of a wedge ensures the blood supply to the antimesenteric border and gives a wider lumen for anastomosis. Continuity of the colon is restored by end-to-end anastomosis and the rectal tube is milked up beyond it. The restored colon is placed behind or in front of the mesentery of the graft as convenient and the loop is washed clean with saline.

The vesical peritoneum is stripped laterally and backwards as far as the superior vesical pedicles which are tied above the ureter. The bladder is opened and all diseased detrusor excised. The colo-vesical anastomosis is made after the manner of Yeates (1956) using interrupted chromic catgut for the outer layer and continuous plain catgut for the through-and-through layer. The incision of the colon is made piece by piece to minimize blood loss from the cut edges. The final closure of the loop brings the opposing cut edges of the colon together. The peritoneal flaps are replaced to cover the new bladder and are tacked to the edges of the mesentery of the loop; tube drainage is provided for each side of the pelvis.

Post-operative care.—The catheter is slung and in the post-operative period it is gently irrigated with sodium bicarbonate solution to remove mucus; no additional suprapubic catheter has been needed. A Ryle's tube is left in position until there are good bowel sounds and the rectal tube is retained until flatus is passed. The catheter is removed in ten to fourteen days. After three weeks the patient is cystoscoped and mucus or sloughs from the suture line are sucked out.

If the ureter has to be reimplanted it is done over a plastic tube which is brought out beside the catheter.

Complications.—The only complication directly related to the operation was in one of the early cases where it had been impossible to restore the peritoneum owing to perivesical infection. The two anastomoses became adherent and a vesicocolic fistula developed; it was closed after temporary colostomy and the man is well eighteen months later. Gil-Vernet and Gosalvez (1957) had 2 cases of fæcal fistula and 2 of urinary fistula which all closed spontaneously. Küss (1958) had 4 temporary urinary fistulæ and 1 colic in 20 cases. In general the post-operative course has been smooth, and in particular there has been no ileus. One man developed intestinal obstruction five weeks after operation but this

was due to radionecrosis of the small intestine which was resected; he remains well four months later.

Results

My personal experience of colocystoplasty comprises 14 cases and whilst this is inadequate for any statistical analysis it has given me some impressions. 7 were for Hunner's ulcer (chronic interstitial cystitis), 2 for contracted bladder following mucosal stripping for papillary carcinoma, 3 for radionecrosis following supervoltage therapy, 1 for long-standing cystitis and only 1 for tuberculous contraction.

All the patients with Hunner's ulcer are doing well. It is important in this condition to remove all the diseased or thickened part of the detrusor and this may be extensive. A woman of 50 who had been treated by periodic distension, cystodiathermy and injection of hydrocortisone for five years still had painful frequency of micturition. Three weeks after colocystoplasty she had no pain and could go for three hours; nine weeks after operation she held 10 oz (300 ml), slept through the night and went for four hours by day. Improvement appears to be rapid and progressive in contrast to the steady deterioration which was the rule under the old method of periodic distension. A universal feature in all the patients has been the abolition of pain, even if the habit of some nocturnal frequency has died hard. The "cottage loaf" type of bladder does not look ideal but its function can be excellent and there is little or no residual urine. It is not always possible to finish with a bladder that has no isthmus. A woman of 51 treated conservatively for three years still had to micturate eight times in the night with considerable pain. Two months after colocystoplasty nocturnal frequency was reduced to once; she had no pain, the bladder held 18 oz (550 ml) and electrolytes were normal. In 1 patient a right ureteric reflux was seen in the cystogram three weeks after operation; the bladder had been excised nearly down to the interureteric bar. It is too early to know if the reflux still persists.

In most patients there is a mild infection of the urine with *B. coli* or enterococci but two had a sterile urine, one as long as ten months after operation.

Severe contraction of the bladder with bilateral reflux follows mucosal stripping for papillary carcinoma even if a cuff is left at the ureteric and urethral orifices, and I have given up this operation. 2 patients developed this complication: in 1 the reflux was diminished three weeks after ureterocolocystoplasty and both blood urea and chlorides were lower; he is being followed-up. In the other I used a closed colonic loop end-to-end twenty months after the original operation. The reflux diminished but his kidneys were too badly damaged and he became uræmic. He recovered with treatment but died from hypertensive heart disease three months after operation. In both cases there was no residual tumour in the bladder.

The radionecrotic bladder is a severe test for any plastic operation and although all three patients now have bigger bladders there is not comparable symptomatic improvement. Much larger replacement rather than mere enlargement is needed in these cases.

Chronic cystitis following long-standing calculous disease in the kidney an l ureter caused pain and incontinence in a man of 34; he wore a urinal. Three months after removing the right ureter and its stone (the kidney having already been removed) I did a colocystoplasty. He had the complications I have mentioned but is now well and the left reflux previously present has disappeared.

There is only 1 case in the series of a contracted tuberculous bladder. A man of 22 with multiple tuberculous lesions and a reflux up the remaining ureter had a fibrotic bladder almost devoid of mucosa of which a large part was cut away during ureterocolocystoplasty. The bladder how looks better and there is no reflux, but he still has frequency.

Conclusions.—Despite a relatively small experience I am convinced that whenever possible the colon is more suitable for enlarging the bladder than the ileum. It is easier to use and the functional results are better both in the force of the stream and the absence of residual urine. The post-operative course is generally smooth.

The best results are obtained by an open flap graft rather than by a closed loop. It is the procedure of choice for resistant cases of chronic interstitial cystitis but has a place in other conditions.

The operation is time-consuming; I agree with Bourque (1959) that it is long, tedious, and must be very meticulous. When doing it I am always reminded of the Song of the Shirt, "Stitch, Stitch, Stitch", but I feel that I shall go on with it.

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Colonic Urinary Conduits

By R. T. Turner Warwick, D.M., F.R.C.S., M.R.C.P.
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The use of segments of sigmoid colon for the construction of urinary conduits is by no means a recent suggestion, but it is a somewhat neglected technique; the fact that colonic mucosa absorbs more fluid, electrolytes and urea than ileal mucosa is of little consequence where a short segment is used as a conduit rather than a reservoir, because the urine is expelled before significant reabsorption can take place. Whether a segment of small or large bowel is used for a urinary conduit is usually optional, but may depend upon the particular case for which this method of diversion has been chosen.

One of the most obvious indications for the use of colon for a conduit is the separate diversion of urine and fæces required, if a wet colostomy is to be avoided, by pelvic exenteration or permanent destruction of both bladder and rectum. Under these circumstances the distal colon has, of necessity, to be divided and the construction of a urinary conduit from it is much less time consuming than from ileum; in most cases it can readily be performed at the end of a somewhat prolonged radical operation.

The stages of this operation are illustrated in Figs. 1 and 2. In this particular procedure the colonic conduit is exteriorized on the right because the colostomy is on the left; if urine alone is to be diverted it is usually more convenient to make the colonic conduit stoma on the left.

The basic principles involved in the construction of a colonic conduit are self-evident: (1) Preoperative bowel preparation is more important than for an ileal conduit. (2) The vascular supply pattern of the colon must be carefully assessed with regard to both the isolated segment and the colonic re-anastomosis. (3) The conduit should be as short as possible and without redundant loops in which urine may pool. (4) The exact site of the stoma is, of course, best assessed preoperatively in relation to the appliance; stomal stenosis must be avoided and excision of the umbilicus facilitates daily toilet.

The details of this procedure have been discussed elsewhere (Turner Warwick, 1959), and only a few selected points in regard to urinary conduits will be considered here.

I suggest that there is considerable advantage in making a urinary conduit, colonic or ileal, extra-peritoneal in so far as possible (Fig. 4): (1) The risk of post-operative adhesions and intestinal loop obstruction is minimized. (2) The vascular pedicle and the ureteric anastomoses are protected at any subsequent abdominal operation. (3) The conduit is relatively fixed in an optimal, high, transverse position and does not sag to form redundant loops (Fig. 5).

When the conduit is to open on the right side

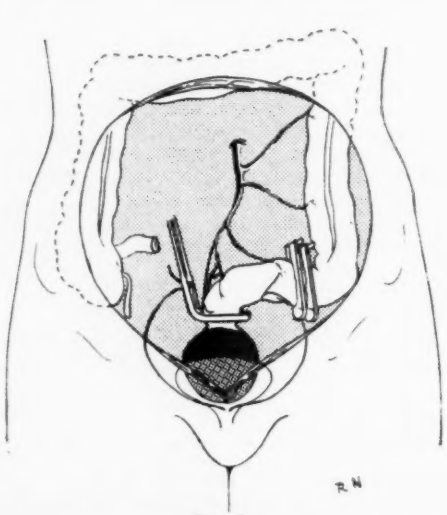

Fig. 1.

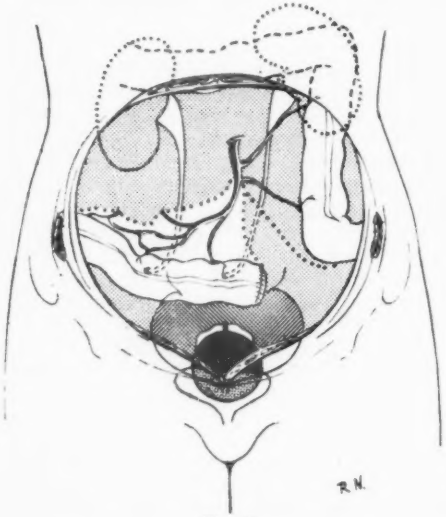

Fig. 2.

Figs. 1 and 2.—A technique for the separate diversion of urine and fæces.

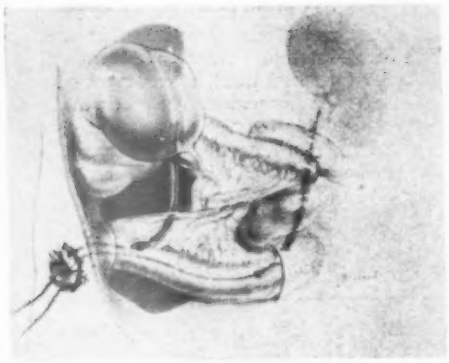

FIG. 3.

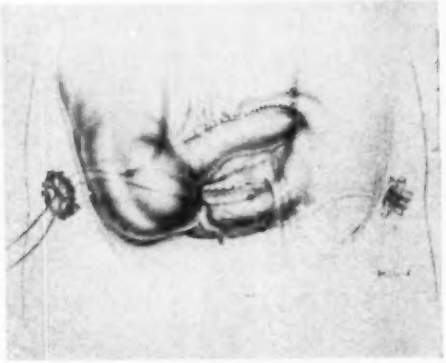

FIG. 4.

FIGS. 3 and 4.—The construction of a largely extraperitoneal ileal conduit.

of the abdomen the cæcum is freely mobilized in the early stages of the operation and the peritoneum lateral to it is undermined with the fingers so that the conduit reaches the surface lateral to the paracolic gutter (Fig. 3). At the conclusion of the operation the cæcum is allowed to overlie the conduit and the closed end of the conduit is tucked under the inferior mesenteric vascular pedicle to overlie the left ureteric anastomosis (Fig. 4).

When the conduit is to open on the left side of the abdomen the peritoneum lateral to the inferior mesenteric vessels is under-tunnelled to the intended site of the stoma in order to receive the conduit.

Conduitography is often informative; the X-ray of an ileal conduit shown in Fig. 5 demonstrates several points: (*a*) The conduit has become grossly redundant although at the time of the operation its length was not considered excessive. (*b*) There is ureteric reflux. (*c*) The "free" polythene splints used for the ureteric anastomosis are still in position, although the operation was performed several months previously; this is an undesirable, but not uncommon, result of this technique.

It is generally accepted that uretero-conduit anastomoses should be direct—that is, allow free reflux—in order to minimize the risk of the much more serious complication of stenosis at the site of the anastomosis. Direct anastomosis is inevitable if the ureter is much dilated, but when the ureter is normal it is perhaps better to perform an indirect anastomosis in an attempt to prevent reflux of conduit urine, which is usually infected.

A simple indirect technique, suitable for ureterosigmoid and uretero-colo-conduit anastomoses, can be made by pulling a short length of

FIG. 5.—A redundant and sagging intraperitoneal ileal conduit.

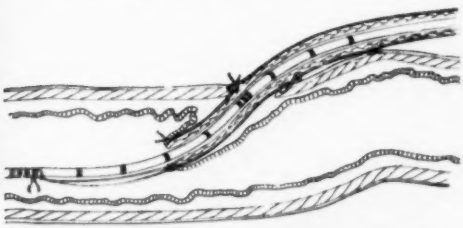

FIG. 6.—A technique of uretero sigmoidostomy.

ureter into the lumen of the bowel after it has been anastomosed to a mobilized pout of colonic mucosa—thus the end of the ureter forms a mucosa-covered, intraluminal, nipple-like projection which prevents reflux and does not tend to stenose (Fig. 6). This pull-in anastomosis is greatly facilitated by the use of ureteric catheter splints which are exteriorized through the conduit (or anus) and removed about the fifth post-operative day; each is anchored to the extreme edge of its ureter (usually between the 15 cm and 20 cm mark) by a fine suture tied with a 2 cm spacing loop to allow some degree of independent movement of the catheter. The ureteric catheters drain into bottles and, therefore, an appliance (or rectal tube) is unnecessary in the early post-operative period. An alternative technique is used for indirect uretero-ileal conduit anastomosis; that described above is unsuitable because the mucosa of this part of the bowel is relatively friable and fixed.

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Section of Comparative Medicine

President—M. CRAWFORD, M.R.C.V.S.

Meeting
March 16, 1960

DISCUSSION ON MAGNESIUM METABOLISM IN MAN AND ANIMALS

Dr. Ruth Allcroft (Weybridge):

Hypomagnesæmia in Cattle and Sheep

Incidence

Cattle.—A metabolic disorder in cows known as "kopziekte" (head disease) was recognized in the Netherlands for about thirty years before Sjollema and Seekles (1929) associated it with low serum magnesium and calcium values; they related an increased incidence in the 1920s to changes in feeding and methods of manuring. Seekles *et al.* (1930) introduced the term "grastetanie" for "kopziekte" as being more indicative of the nature and cause of the disorder.

An acute metabolic disturbance of lactating beef cows was recognized in the Border Counties as "lactation tetany" (Lothian, 1931) and in the South West of England as "Hereford disease". In a detailed description of the condition as it occurred in Britain, Dryerre (1932) noted that the only consistent abnormality found in the blood of affected animals was a low magnesium content sometimes but not always associated with a low serum calcium level.

In spite of objections by Dryerre (1932) and Barker (1932) that the terms "lactation tetany" and "grass tetany" were unsuitable because occurrence was not limited to lactating cows or to cows at grass, and because the condition was characterized by convulsions rather than tetany, the word "tetany" is now used almost universally.

Hypomagnesæmic tetany has been reported in most European countries, in New Zealand, North America and Australia. The incidence of the disease in Britain is not accurately known but recent surveys of dairy herds indicate annual losses of about 0·5%; losses in beef herds and in suckling calves have not been assessed. There is general agreement that the incidence has increased steadily over the last fifteen years. In the Netherlands 1 to 2% of 1,500,000 dairy cattle are affected yearly (Seekles, 1958). Although the incidence is lower than that of milk fever (hypocalcæmia) or ketosis, it is sufficiently high to be of economic importance, chiefly because the death-rate is much higher than in the other two metabolic disorders. Hypomagnesæmia is often unsuspected until sudden and unexpected deaths occur.

Cattle of most European breeds of either sex and of all ages can be affected but it is most common in lactating cows, the incidence being greatest in the two months after calving; suckling beef calves of 3 to 6 months of age are also frequently affected. Occurrence is most common in dairy cows during spring and autumn periods of rapid growth of grass, and in out-wintered beef cattle and young stock during the winter and early spring months when there is little growth of grass. Hypomagnesæmia can, however, occur at any time in stalled or grazing animals under most conditions of management.

Sheep.—There is little definite evidence of hypomagnesæmic tetany in sheep before Stewart (1952) described its sudden and widespread occurrence in Scotland. It has since occurred frequently amongst both hill and lowland flocks of all breeds throughout Britain; it has also been recorded in Ireland and North America. No assessment of the incidence in sheep has been made but there is no doubt that it has increased in Britain over the last ten years. The highest incidence occurs in ewes with twin lambs during the four weeks after parturition, usually when the flock has been moved on to a "good" pasture.

Horses.—A "transit tetany" which occurred in Welsh mountain ponies taken from their grazing and transported by rail was reported by Montgomerie *et al.* (1929). Suckling mares were also affected soon after being housed. Green *et al.* (1935) found a pronounced hypomagnesæmia as well as hypocalcæmia in affected ponies.

Clinical Picture

The clinical picture consists essentially of hyperexcitability, muscular tremors and convulsions. The first signs are usually those of apprehension. The animal is nervous and excitable, the head is held high and the eyes often have a staring expression; there is twitching of the muscles, especially of the face and ears; limb movements are stiff and exaggerated and the animal frequently hesitates and staggers when walking. In acute cases, extreme excitement and violent convulsions develop soon after the onset of initial signs, and if treatment is not given, exhaustion and death quickly follow. Death may even occur so rapidly that the animal is found dead without any symptoms having been noticed. A chronic form, characterized by a stiff gait and gradual loss of condition may exist for

several weeks without affecting appetite or milk yield; this is followed either by recovery or by the signs of acute disease.

Preconvulsive signs in sheep are less clearly defined than in cattle and may easily be confused with those of hypocalcæmia or of pregnancy toxæmia. An affected ewe usually stands apart from the rest of the flock with head down, and if made to move, will stagger and fall down in convulsions.

Post-mortem findings are often negative but in cattle there are usually subserous hæmorrhages on the epicardium, the aortic arch and abdominal organs.

Pathogenesis

The characteristic abnormality is a low blood magnesium level at the time of onset of symptoms. The accepted normal range for serum magnesium in cattle and sheep is 1·8 to 3·2 mg/100 ml. Clinical signs are likely to occur when the serum magnesium value falls below 1 mg/100 ml, but they may be found at levels of 1·0–1·7 mg/100 ml. A concomitant hypocalcæmia is frequently present (Sjollema, 1930; Allcroft, 1947*a*) and sometimes acetonæmia also (Gerring, 1954).

There are two main types of hypomagnesæmia: (1) An acute form in which the level of serum magnesium falls rapidly within a day or two. This is common in milking cows turned abruptly from stall to pasture. (2) A slowly developing form in which the fall is gradual throughout the autumn and winter. This type is most common in out-wintered stock which may show no clinical symptoms even though blood magnesium levels are low. In calf tetany, the fall in serum magnesium is gradual; clinical symptoms do not usually appear before eight to twelve weeks.

In hill sheep there is considerable fluctuation in serum magnesium and calcium levels throughout the gestation and suckling periods of winter and spring; again, persistently low magnesium values (0·7 to 1·7 mg/100 ml) may be present without any clinical abnormalities.

Causation

There is still little agreement as to primary physiological causes of hypomagnesæmia. Because this can occur under such a variety of conditions, and because within an affected herd it is usual for only a few individuals to show clinical symptoms of the disease, some workers regard the magnesium content of the diet as being of little importance. Further evidence is to be found in the rapidity of the fall in serum magnesium and the suddenness of onset of symptoms in cows on spring grass, suggesting that a dietary deficiency of magnesium in the classical sense cannot be the whole explanation, and in the fact that pastures and rations on which hypomagnesæmia occurs frequently have a normal or high magnesium content. Green (1948) postulates that the disease is a physiological dysfunction of neural and endocrine mechanisms affected by environmental stresses. Others, especially the Dutch workers, hold that diet is a most important factor but that this is not necessarily related to a low magnesium intake (Sjollema and Seekles, 1933; Brouwer, 1952; Kemp and 't Hart, 1957).

The increased incidence of grass tetany in the Netherlands has for some time been associated with fertilizer treatments of the pasture. Kemp and 't Hart (1957) reported that only on pastures where potassium manuring was excessive was the incidence of tetany high, and that the addition of nitrogen further increased the incidence. British work has also shown a relationship between tetany and heavy dressings of nitrogenous fertilizers, alone (Bartlett *et al.*, 1954) or with potash (Smyth *et al.*, 1958; Burns and Allcroft, 1959).

Since fertilizer treatment and incidence of tetany are not constantly associated with a reduction in the magnesium content of the pasture, it is possible that other changes in herbage composition may influence absorption or utilization of magnesium by the animal. Rook and his colleagues (Rook and Balch, 1958; Rook, Balch and Line, 1958) related hypomagnesæmia in milking cows to a reduction in the dietary supply of "available" magnesium on the change from winter rations to spring grass, but Field *et al.* (1958) found no reduced availability for sheep of magnesium of grass from fields in which hypomagnesæmic tetany had occurred in grazing cows. The sheep, however, showed a marked difference in their metabolism of the same amount of magnesium. Work in Norway (Breirem *et al.*, 1949) and New Zealand (Swan and Jamieson, 1956) suggests that if the rations are deficient in energy, higher intakes of magnesium are required to maintain normal serum magnesium levels.

It would seem that the slowly developing hypomagnesæmia in outwintered stock may be related to a low intake of both magnesium and energy-supplying foods. The nutritional level is frequently low over this period and clinical symptoms are often precipitated by wet, cold weather when loss of body heat is greatest. Allcroft (1947*b*) and Inglis *et al.* (1954) showed that supplementary feeding with hay or cabbages can prevent this hypomagnesæmia. Blaxter (1954) attributed the hypomagnesæmia of the calf to a simple dietary deficiency, but Smith (1957) considered that a milk diet provided more than adequate magnesium and that hypomagnesæmia was due to a progressive decrease in the ability to utilize dietary magnesium.

Whatever the causes of hypomagnesæmia, there

is now ample evidence that adequate dietary supplements of suitable magnesium compounds will prevent a severe fall in the serum magnesium level, and prevent the development of clinical symptoms (Blakemore and Stewart, 1935; Allcroft, 1954; Seekles, 1958). Since it is difficult to ensure adequate oral supplementation in grazing animals, control has also been effected by raising the magnesium content of heavily fertilized pastures by top-dressing with magnesium oxide or magnesian limestone (Bartlett *et al.*, 1954; Parr and Allcroft, 1957).

Although preventive measures may be applied at the soil, plant, or animal level, complete and satisfactory control of the disease is not possible without more knowledge concerning the dietary and physiological factors which affect absorption and utilization of magnesium in the ruminant.

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Dr. Iain MacIntyre (London):

We know very little about magnesium metabolism and magnesium deficiency in man: in this paper I shall summarize some recent work bearing on the physiology of magnesium in man and animals, and on the syndrome of magnesium deficiency in man.

The Interrelation of Calcium and Magnesium Absorption

Berglund and Forster (1958) studied the aglomerular marine teleost, *Lophius americanus*. They suggested that a separate transport system for divalent cations must exist to explain their finding that the divalent cation with the higher excretion rate depressed competitively transfer of the other. Alcock and MacIntyre (1960) carried out complete balance studies in the normal, magnesium-deficient and calcium-deficient rat. This was accomplished by tube-feeding a diet of known calcium and magnesium content (Hanna and Alcock, 1960), which also contained a constant and known amount of chromium sesquioxide. This substance is not absorbed from the gut, and if its concentration in the fæces is known, then total fæcal excretion of calcium and magnesium can be readily calculated.

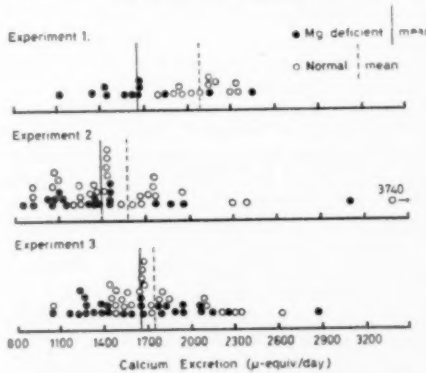

Fig. 1.—The fæcal calcium excretion in magnesium-deficient and normal rats. The figure is a scatter-diagram of the daily calcium excretion in the fæces of individual rats in three separate experiments.

Fig. 1 shows that in the magnesium-deficient rat, the fæcal excretion of calcium was significantly lower ($P < 0.01$, analysis of variance) than in rats receiving normal amounts of calcium and magnesium. Conversely, in the absence of calcium

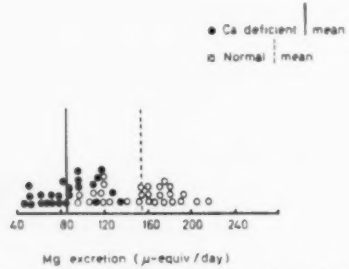

FIG. 2.—The fæcal magnesium excretion in calcium-deficient rats.

from the diet, less magnesium was excreted than normal (Fig. 2). The net absorption of calcium in the magnesium-deficient animal was equivalent to the total amount of calcium and magnesium absorbed in the normal group. Urine was also collected in these experiments, and it was found that, from the first day of magnesium deficiency, urinary excretion of calcium was diminished, despite the presence of hypercalcæmia. No change in the glomerular filtration rate was detected, and it seemed probable that the decreased urinary excretion of calcium was due to an increased absorption of filtered calcium by the renal tubular cells.

These results were most readily explained by assuming that a common transport system for the absorption of calcium and magnesium exists, not only in the gut, but also in the renal tubule. This hypothesis is in accord with the *in vitro* experiments of Schachter and Rosen (1959). These workers showed that, in the isolated rat, rabbit and guinea-pig gut, transport of calcium was depressed in the presence of magnesium ions. Further strong evidence in favour of the existence of a common gut transport system for calcium and magnesium has been provided by experiments carried out by Dr. Ruth Allcroft. She was able to show that addition of calcium lactate to the diet of calves, exclusively fed on milk, caused the expected hypomagnesæmia to occur earlier, and become much more profound. Perhaps hypomagnesæmia in the milk-fed calf is to be regarded as a conditioned deficiency of magnesium, due to an abnormally high calcium intake.

That these observations may be relevant in man is suggested by the metabolic data presented in Fig. 3. This shows studies carried out on a case of idiopathic steatorrhœa with hypomagnesæmia. These studies were carried out in collaboration with Dr. C. C. Booth and are being presented in more detail elsewhere (MacIntyre *et al.*, 1961). Calcium and magnesium balances were carried out in the Metabolic Unit of the Hammersmith Hospital: first, on a low calcium intake; next, on a high calcium intake; and finally on a high calcium and magnesium intake. It can be seen that the hypomagnesæmia is to be attributed to a negative magnesium balance, and that this negative magnesium balance became more marked on the high calcium diet; a positive magnesium balance was only induced by a very large increase in the magnesium intake.

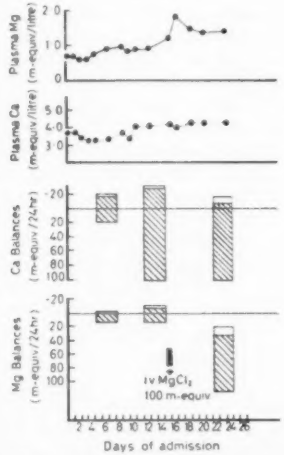

FIG. 3.—Calcium and magnesium metabolic data in a case of idiopathic steatorrhœa. Balances charted by the method of Reifenstein *et al.* (1945).

Magnesium Deficiency in Man

The syndrome of magnesium deficiency in man has been described by Hanna *et al.* (1960*a*). It is made up of the following features: (1) Liability to epileptiform convulsions. (2) Depression, vertigo, ataxia and muscular weakness. (3) A low voltage ECG. (4) A positive Chvostek sign together with a negative Trousseau sign.

It should be emphasized that tetany, in the sense of painful peripheral muscle spasms, is not a feature of magnesium deficiency. Greenberg and Tufts (1938) noted that magnesium deficiency in the rat was clinically quite different from hypocalcæmia, although they continued to use the term tetany to describe both. It seems likely that this usage has been responsible for some clinical confusion. Blaxter (1956) and Brandt *et al.* (1958) have regarded the skeleton as a magnesium reservoir, readily drawn upon in case of need, and adequate to prevent depletion of the body cells. However, MacIntyre and Davidsson (1958) showed that, although the femur magnesium concentration declined in the growing magnesium-deficient rat, there was little or no change in the total magnesium content in the femur. It was also found that there was a

decline in magnesium concentration in skeletal muscle, in contradiction of some earlier findings. This discrepancy was probably explained by the fact that MacIntyre and Davidsson used a specific flame-spectrophotometric method of analysis and expressed the results in terms of dry fat-free muscle solids. Involvement of the body cells in magnesium deficiency in man, with unavailability of the skeletal magnesium, was demonstrated in the case illustrated in Fig. 3: biopsies showed that the muscle magnesium content was reduced to 47 mEq/kg of dry fat-free solids (normal 63–78) although magnesium concentration was 191 mEq/kg dry fat-free bone (normal 212–233). It seems that the concept of the skeleton as a magnesium reservoir should be discarded, and that it should be recognized that magnesium deficiency, whether occurring in man or in the experimental animal, involves the cells.

In view of the rapidity of renal damage produced by magnesium deficiency in the experimental animal (Hess *et al.*, 1959), it would be reasonable to treat hypomagnesæmia in man, even if it had not been shown that severe deficiency involves a liability to potentially fatal convulsions. Hypomagnesæmia should be sought, and if found effectively treated, in the following clinical conditions, where our recent experience shows that it may sometimes occur: (1) The malabsorption syndrome. (2) Hyperparathyroidism (especially post-operatively) (Hanna *et al.*, 1960*b*). (3) Renal tubular syndromes with electrolyte loss. (4) Prolonged fluid and electrolyte loss from any source. (5) Primary aldosteronism.

No doubt as we learn more of magnesium metabolism in disease in man, by the more widespread use of satisfactory methods of analysis, many of our present concepts and conclusions will require expansion or alteration; it seems unlikely, however, that future work will modify the main conclusion from the work described above. This is: the similarities in man, livestock and the experimental animal in magnesium metabolism, and in the syndrome of magnesium deficiency, are far more striking than their differences.

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Professor A. Robertson (London) also took part in the discussion.

Meeting
April 20, 1960

DISCUSSION ON THE PHYSIOLOGY OF THE NEW-BORN MAMMAL

Professor R. A. McCance (Cambridge) opened the discussion with a review of *Somatic Stability in the Newly Born* (*see Arch. Dis. Childh.*, 1959, **34**, 361, 459).

Dr. G. S. Dawes (Oxford):

Anoxia and Survival after Birth

The object which my colleagues and I have had in mind in working on acute anoxia at birth has been to discover what factors limit survival, and to find out whether it is possible so to modify them that survival may ensue after a period of anoxia which would otherwise be fatal, or which would have caused permanent cerebral damage.

We decided to employ total asphyxia or anoxia in fœtal and new-born animals, because it is then comparatively easy to reproduce standard experimental conditions. It is well known that immature fœtuses, and the young of species which are born in an immature state, can survive total anoxia for a time which would kill an adult of the same species subjected to this treatment. For instance animals such as kittens, puppies and rats are very difficult to drown at birth, and they will recover completely if exposed to air before the last gasp. Rats 3 weeks old survive only two to three minutes in nitrogen. Some species, such as the guinea-pig, are more mature at birth, and the young do not live for more than a minute or two longer than the adult in nitrogen. Human infants at birth appear to be intermediate between rats and guinea-pigs in this respect. The ability of new-born rats to survive so long has been attributed to their ability to derive energy with

which to maintain cell integrity, the "ionic pumps" which keep the internal cell environment constant, by anaerobic glycolysis (i.e. by breaking down carbohydrate to 3-carbon residues such as lactic and pyruvic acid). Thus Himwich *et al.* (1942) showed that the ability to survive prolonged anoxia was abolished on injection into new-born rats of iodoacetate, which inhibits glycolysis. The energy derived from anaerobic glycolysis of a molecule of glucose is very much less than that derived by aerobic breakdown to CO_2 and water, and this process would be expected to be limited by the availability of carbohydrate, and by the fall of pH which ensues when acid metabolites are allowed to accumulate in the body.

Effect of environmental temperature.—At low body temperatures and in anoxic conditions, in which cold does not cause an increase of metabolic rate, chemical reactions proceed more slowly, and therefore new-born animals live longer. There is a large literature on this subject, to which I need not refer. Our primary concern has been to standardize experimental conditions and thus to investigate the other variables which may limit survival. Therefore all the experiments which we have carried out have been at body temperatures which have been kept as constant and as near to the normal as practicable.

It is evident that there are at least two factors concerned in the unusual ability of the very young animal to survive anoxia. I shall distinguish these, arbitrarily, as the "tissue factor" and the "circulatory factor" respectively. In the whole animal these factors combine. They can be separated in the following ways. If the circulation is arrested, gasping may continue for up to twenty minutes in the new-born rat (Himwich *et al.*, 1942) and six to ten minutes in the anæsthetized fœtal monkey (Dawes *et al.*, 1960), yet this is rather less than half the time to last gasp of the intact animal asphyxiated under similar conditions. These observations show both that the respiratory centre can continue functioning for a surprising length of time in the absence of the circulation, and also that in its presence gasping continues for very much longer. It seemed to us that the physiological changes in the circulation might provide a model of what was going on elsewhere during anoxia, and that if we could in some way prolong the function of the cardiovascular system, the first step might have been taken towards prolonging the survival of the whole animal.

Experiments on anæsthetized fœtal lambs were therefore begun, and it was found that the duration of survival, as judged by the fall of blood pressure and heart-rate, was directly related to the initial concentration of glycogen in the cardiac ventricles. The quantity in the liver did not appear to affect the issue. A direct relationship between cardiac glycogen and the time to last breath in total anoxia was also demonstrated in new-born rats, rabbits and guinea-pigs (Dawes *et al.*, 1959) and also in fœtal and new-born monkeys (Dawes *et al.*, 1960). As these animals grow the concentration of glycogen in the heart, which may exceed 30 mg/g, falls towards the adult level of less than 5 mg/g, and the ability to survive anoxia falls *pari passu*. Perhaps the most striking demonstration of this relationship is some experiments by Stafford and Weatherall (1960) in rats. The glycogen concentration of the cardiac ventricles was found to alter with age, with a short period of fasting or on subjection to a period of anoxia just short of lethal. Under all these circumstances the time to the last gasp during a subsequent period of anoxia was directly related to the cardiac glycogen concentration in similarly treated littermates. Again, the carbohydrate content of the liver, which was often much greater than that of the heart, did not appear to influence the result. The inference was drawn that liberation of glucose from the liver was a factor of only secondary importance with regard to survival in these particular experimental conditions.

With these considerations in mind a series of experiments was begun, two years ago, to see whether survival could be prolonged in fœtal lambs subjected to acute anoxia.

The experiments, which were done in collaboration with Dr. J. C. Mott and Dr. A. Stafford, were begun on anæsthetized lambs which were less than two-thirds of the way through gestation and which could not expand their lungs. Intravenous infusion of glucose alone did not prolong survival, as judged by the blood pressure and heart-rate. Infusion of alkali alone to keep the arterial pH from falling during anoxia also did not prolong survival. But when glucose and sodium carbonate were administered together, the time taken for the blood pressure to fall from the initial level of 30–40 mm Hg down to 10 mm Hg was increased from a mean of forty-eight minutes to more than eighty minutes. In the treated lambs the heart-rate was also much greater. This treatment was also effective in raising the blood pressure and heart-rate even when it was delayed for as long as forty minutes after the cord had been tied.

A further series of experiments on the therapeutic effect of glucose and alkaline infusions was also carried out on mature lambs, within a few days of term. These lambs were delivered by Cæsarean section under anæsthesia, and the head

was covered by a saline-filled bag to prevent inhalation of air. The umbilical cord was tied and asphyxia produced for ten to fifteen minutes. When treated lambs were compared with untreated twins it became clear that infusion of sodium carbonate and glucose altered the course of events. In the treated lambs the blood pressure and heart-rate were higher at the end of ten minutes' anoxia, respiratory movements continued for longer and recovery was more rapid. Whether cerebral damage, short-term or permanent, was prevented could not be determined, because the difference between treated and untreated lambs was not great, and because criteria for the assessment of cerebral damage in the new-born lamb are not yet properly established. A caution must be given: these results were obtained with continuous intravenous infusion from the onset of anoxia, at a rate which increased the blood glucose considerably and which maintained the arterial pH at a relatively high level. The latter in particular is not easy to achieve in practice. Therefore, although these results are promising, they do not as yet justify application to the human infant. What they do show is that the problem of treatment of anoxia at birth may not be hopeless, and they suggest that systematic analysis of the other physiological changes which occur in this condition is worth while.

To summarize, we believe that the ability of the very young animal to survive prolonged asphyxia depends on two factors. As to the "tissue factor" there is no evidence available of the critical biochemical difference between young and adult tissues. The "circulatory factor" would appear to depend on the greater glycogen reserves of the heart in immature animals and perhaps also on the effect of the "tissue factor" in the heart itself. We do not know how the glycogen reserves are accumulated.

There is therefore a wide field for further research on the fundamental physiology of this subject, quite apart from the applied physiology on which future methods of treatment may be based.

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Dr. K. W. Cross (London):

The Gasp of the New-born Infant in Response to Inflation of the Lung [*Summary*]

It has been known since 1868, when Hering and Breuer described the effects of inflation and deflation of the lung, that the normal, adult response to lung inflation is a cessation of inspiratory activity. Head, however, in 1889 described a special circumstance when the response to lung inflation might be an active inspiratory effort. This occurred in the rabbit whose vagi had been cooled until they had ceased to conduct afferent impulses from the lung. As the vagi warmed, but before all the fibres were conducting, there was an intermediate phase when inspiration followed inflation. This response has become known as Head's paradoxical reflex.

My colleagues and I have studied the response of the new-born baby to lung inflation with air in an attempt to devise a method for measuring the cardiac output in the baby (by the method of Lee and DuBois, 1955). Surprisingly, the sleeping new-born baby accepts lung inflation very readily; very frequently, particularly in babies less than 24 hours old, there was an active inspiratory gasp before a period of apnœa. This gasping response diminishes with age. It is interesting to speculate whether this gasp may be part of the reflex which is responsible for the original expansion of the lungs in the new-born.

This work is described in greater detail in the *Journal of Physiology* (Cross *et al.*, 1960).

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Meeting
May 20, 1960

A JOINT MEETING was held with the Section of Epidemiology and Preventive Medicine when a discussion took place on **Myxomatosis in Britain.** A general introduction was given by Dr. C. H. ANDREWES, Mr. H. W. THOMPSON spoke on **Epizootiology** and the Hon. MIRIAM ROTHSCHILD on **Entomological Aspects.** Mr. M. CRAWFORD, President of the Section of Comparative Medicine, was in the Chair.

Meeting
June 15, 1960

Meeting Held at the Institute of Animal Physiology, Babraham Hall, Babraham, Cambridge

The following demonstrations were given:

EEG in the Sheep. The characteristics of some points of cardiovascular and respiratory representation in the cerebral cortex of sheep.—Dr. J. F. Mitchell (1958, *J. Physiol.*, **143,** 17P).

Proteinuria in the New-born Calf.—Dr. A. E. Pierce (1959, *J. Physiol.*, **148,** 469).

Isolated Perfused Goat Udder. The rate of incorporation of ^{32}P into milk and casein by the perfused udder.—Dr. D. C. Hardwick and Dr. J. L. Linzell (Hardwick, D. C., Linzell, J. L., and Price, S. M., 1960, *Biochem. J.*, **75,** 5P). Some factors affecting milk secretion by the perfused mammary gland.—Dr. D. C. Hardwick and Dr. J. L. Linzell (1960, *J. Physiol.* (in press).

Ataxia in Hens (short film). Ataxia in hens poisoned by tri-para ethylphenylphosphate.—Miss A. Silver (1960, *Nature, Lond.*, **185,** 247).

Metabolism of the Piglet. The metabolic rate of the new-born pig in relation to environmental temperature and to age.—Dr. L. E. Mount (1959, *J. Physiol.*, **147,** 333).

Thermal Regulation in the Sheep. The receptors concerned in the thermal stimulus to panting in sheep.—Dr. J. Bligh (1959, *J. Physiol.*, **146,** 142).

Methods of Studying Ruminant Digestion. Collection of pancreatic juice from the conscious sheep.—Mr. K. J. Hill (Hill, K. J., and Taylor, R. B., 1957, *J. Physiol.*, **139,** 26P).

Rumen Oligotrich Protozoa.—Dr. G. S. Coleman (1958, *Nature, Lond.*, **182,** 1104; 1960, *J. gen. Microbiol.*, **22,** 555).

Fat Metabolism in Ruminants.—Dr. D. B. Lindsay.

Intracellular Localization of Neurohumours.—Dr. V. P. Whittaker (1959, *Biochem. J.*, **72,** 694; 1960, *J. Physiol.*, in press).

Applications of Gas Chromatography.—Dr. P. F. V. Ward (1960, *Biochem. J.*, in press).

Protein Metabolism in Rumen.—Dr. J. L. Mangan (1959, *N.Z. J. agric. Res.*, **2,** 990).

Serum and Tissue Enzyme Levels in Liver Disease.—Mr. E. J. Ford and Mr. J. W. Boyd (1960, *Res. vet. Sci.*, **1,** 232).

A Monolayer of Lecithin Hydrolysed by α Toxins of *Cl. welchii*.—Dr. A. D. Bangham and Dr. R. M. C. Dawson (1959, *Biochem. J.*, **72,** 493; 1960, *Biochem. J.*, **75,** 133).

Incompatibility of Sheep Blood.—Sir Alan Drury and Dr. E. M. Tucker (1958, *Immunology*, **1,** 204).

Aldosterone in Red Cells and Plasma.—Dr. M. Holzbauer and Dr. M. Vogt.

Indole Compounds in Cerebrospinal Fluid.—Dr. G. W. Ashcroft and Mr. D. F. Sharman (1960, *Nature, Lond.*, **186,** 1050).

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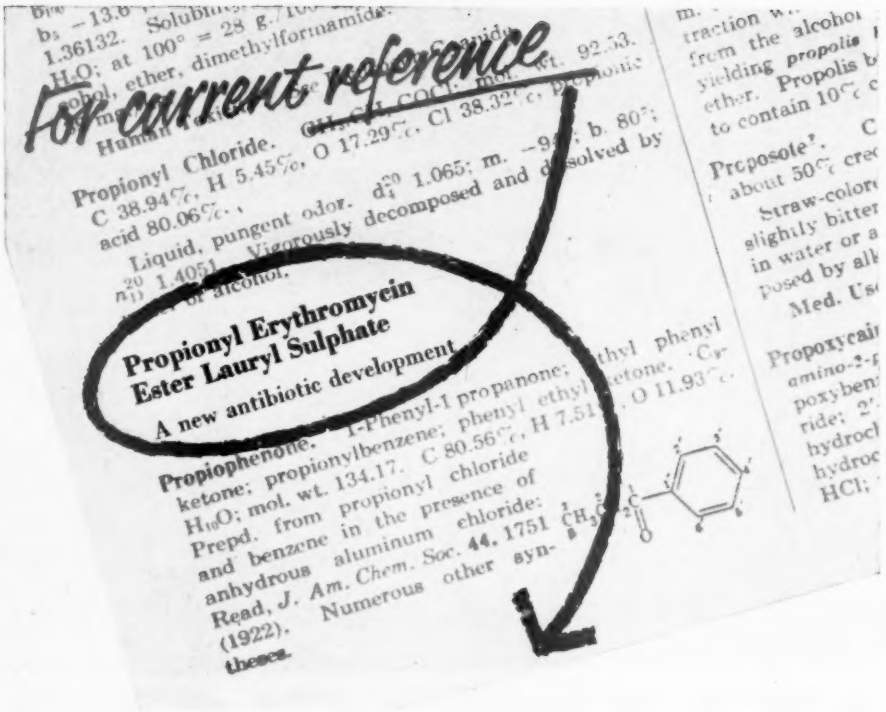

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Meeting
March 10, 1960

A DISCUSSION was held on the **Complications of Intra-ocular Surgery.** The opening speakers were: Mr. H. B. STALLARD on **The Complications of Glaucoma Surgery;** Mr. O. M. DUTHIE on **Post-operative Intra-ocular Infection;** and Mr. J. R. HUDSON on **Cataract Extraction.**

Meeting
May 12, 1960

A DISCUSSION was held on the **Treatment of Tumours of the Eyelids.** The opening speakers were: Mr. F. D. MCAULEY and Dr. KENNETH NEWTON, who spoke on **Implantation and Irradiation;** and Mr. JOHN WATSON, who spoke on **Surgery.**

Subsequent speakers included Mr. H. B. STALLARD, Mr. PETER A. ROGERS and Dr. J. L. REIS.

Meeting
June 9, 1960

The Heritage of Gonin

By Professor MARC AMSLER
Zürich, Switzerland

JULES GONIN of Lausanne died at the age of 65, on June 10, 1935, twenty-five years ago tomorrow. It is the imminence of this anniversary that has dictated my choice of subject. I shall first enumerate the bequests left by the Master of Lausanne on his death, and then examine how this heritage has been developed during the last quarter of a century.

But first of all let us recall how detachment of the retina was treated before the days of Gonin.

Men of my age can remember that the arrival in hospital of a patient suffering from detachment meant the occupation of a bed for weeks or months to no purpose, despite immobilization in the supine position, pressure bandaging, scleral puncture, Deutschmann's discission of the vitreous, subconjunctival or intra-vitreous injections or pilocarpine sudations.

I well remember a case of detachment of the retina, with an extensive tear of some few hours' standing, in which my first teacher in ophthalmology, Professor Eperon (Gonin's predecessor at Lausanne), decided to do nothing because, in the language of those days, "the retina was not only detached, but also torn". That was in 1917 or 1918.

At that time there was much talk of a recent survey carried out by Vail, of Cincinnati, in 1913: about 20 successful results were reported from 25,000 cases of detached retinæ and this was the lamentable figure quoted from the clinical experience of 281 eminent American ophthalmologists. I reproduce some of their answers to a questionnaire:

> "Rest and let alone is the treatment. I consider anything else charlatanism."
> "Dark room, rest in bed, head depressed, tight bandage, resignation."
> "In two years in Vienna and London and three years at the New York Eye and Ear Infirmary, I have never seen a detachment cured."
> "I consider a detachment of the retina a hopeless condition."
> "From kali-iodate to Deutschmann not a single case of permanent cure!"

Impressive documents of the pre-Gonin epoch, are they not?

And Vail concludes: "The established medical treatment of detached retina is a failure, because the etiology of the trouble is not recognized; the surgical treatment is not founded on scientific principles and is therefore brutal; detachment of the retina is not a disease but a symptom. . . ."

It was in almost identical terms that Gonin had closed his chapter devoted to detachment of the retina in the sixth volume of the "Encyclopédie Française d'Ophtalmologie" which appeared in 1906.

Gonin's Bequests and Principles

The *first bequest* of Gonin's legacy was an absolute necessity: the necessity of making a thorough methodical and patient ophthalmoscopic examination of the peripheral retina.

How right the man was who said after watching the master at work: "But Gonin's specific instrument is not the thermocautery, it is the ophthalmoscope"; and I can still hear an old German Professor of Ophthalmology coming out of the dark room with Gonin, saying: "Wir müssen spiegeln lernen"—we must learn to use the ophthalmoscope.

Gonin taught us to explore the peripheral retina as far as the pigmentary edge of the ora serrata through the pupil in extreme mydriasis. He had pinned an attractive group of butterflies (caught by himself on Sundays) on the ceiling of his consulting room, and on these the patient had to fix his gaze tirelessly, so that the master could search for the tear far up in the eye.

It is not without interest to remember that Gonin had been "at home" (so to speak) in the pre-equatorial zone of the retina as early as 1901, when he demonstrated that the extreme peripheral area was free from pigmentation in "retinitis pigmentosa" and that the visual field developed an annular scotoma and did not exhibit concentric contraction from the periphery.

Gonin's *second bequest* to us was his clear perception of an anatomical and clinical fact—the retinal tear and its fundamental importance.

Retinal ruptures, it is true, had been observed before Gonin's time. De Wecker had already noted them in 1870 (the year of Gonin's birth); and in 1882, Leber had been very close to guessing their pathogenic role. But it is certainly Gonin to whom the credit must go for having originated the doctrine (and how fruitful a doctrine!) that any detachment of the retina stems from a break.

It took twenty years of patient labour, ophthalmoscopic observation, histological research and deep clinical thought, to bring my master to a conviction sufficiently strong to persuade his hand to pick up the thermocautery. It was in 1920 that what used to be called Gonin's "idée-fixe" or obsession became an "idée-force" and led him into action.

The old petrol thermocautery had a great virtue in demonstration, a virtue Gonin constantly stressed: either the cautery hit the target of the tear and all detachment vanished; or else it hit to one side leaving all or part of the tear still open, and the detachment remained as before. And it was this demonstration that, in due course, convinced those who were to be the first to adopt the new method of treatment—men such as Arruga, Kapuszynski, Weill, Bruckner and others—men who, at the memorable Amsterdam-Congress of 1929 deeply moved the master by being the first to give him the immense satisfaction of finding himself at last believed and followed.

In the *Lancet* for December 7, 1929, appeared the following few lines—lines which herald a new era: "At the recent International Congress at Amsterdam, Dr. J. Gonin of Lausanne showed paintings of patients treated by a new method designed to close up the hole in the detachment by means of thermocautery, the results being said to be remarkable."

The *third element* in the heritage which Gonin left to us concerns the pre-operative phase of the surgical treatment of detachment.

"Give the patient absolute rest," said Gonin, "lay him down, not always on his back, but lay him—so to speak—on his retinal tear, and you will see the detachment diminish and the retina draw nearer to the choroid. The operative prognosis will be in direct proportion to the speed with which this pre-operative contact between retina and choroid is re-established, for, at the moment of operation, the retina must be as close as possible to the ocular wall." "In the presence of recent detachment of the retina", again I quote Gonin, "one must, of course, act immediately. But this does not refer to the operation; it refers to the need for immediate immobility of the eye and rest for the patient—the immobility and the rest being angled according to the site of the tear". Urgent treatment begins, then, for the patient with several days of preparatory rest and immobility, and for the surgeon by as many days of thorough ophthalmoscopic examination. "We must", Gonin repeatedly said to us, "know the fundus of the eye on which we are to operate *by heart*!"

Gonin's legacy includes, in addition to all this, a fundamental pathogenic concept, that the complex process of tissue degeneration which can result, in myopic or aged eyes, in tearing and detachment of the retina is at the same time a disease of the choroid, the retina and the vitreous body. It is certainly true that the vitreous, by reason of the traction of its pathological adhesions to the retina, plays a particularly important part; this much is evident, from the production of tears with flaps which are by far the most frequent. But the changes in the vitreous are subsidiary, or at any rate bound up with a chorioretinal dystrophy. In any case, it is impossible in any pathogenic conception to separate the retina from the choroid and the vitreous. Thus, idiopathic detachment of the retina is not an illness in itself, but only a more or less acute episode in an eminently chronic degenerative process of the eye.

The *last bequest* left by Gonin was a hope, a hope which I heard him express countless times, a hope the realization of which the pioneer of thermocautery could not even glimpse, the hope of preventive medical treatment for detachment,

or perhaps even of prophylactic surgical intervention.

Later Development of Gonin's Principles

Let us now consider how this rich legacy of Gonin's has fared at our hands during the twenty-five years that separate us from his death.

The insistence on thorough ophthalmoscopic examination of the retinal periphery has lost none of its force; for it is still true—now as always—that tearing starts, and takes place, at the periphery of the retina. The necessity for this examination has somewhat brought back into favour indirect ophthalmoscopy, which Gonin used exclusively, and which lends itself better than direct ophthalmoscopy both to topographic exploration of all the fundus, and to regular ophthalmoscopic checking during operation.

Ingenious electrical instruments have been devised to facilitate this exploration. Schepens' forehead ophthalmoscope in particular deserves special mention, since it leaves the observer a free hand to carry out Trantas' old practice of exerting pressure on the pre-quatorial sclera so as to bring the area of the ora serrata within the ophthalmoscopic field. And this reveals, especially in aphakic eyes, unsuspected hidden lesions in the extreme periphery of the retina. It is again the peripheral retina that we explore with the slit-lamp, and that thanks to the mirrors of Goldmann's contact glass.

Secondly, the primacy of the role of retinal tearing has been, and is constantly being, reaffirmed. No matter what the surgical technique since Gonin's days—whether chemical cauterization, diathermy or electrolysis—the retinal tear must either be reached by the exudative reaction of the choroid and engulfed in the scar, or surrounded by adherent scarring.

Our present surgical procedures are more diffuse in their effects than was Gonin's thermocautery, for his instrument entered the eye at one specific point only. We no longer need such precise initial pin-pointing as that required by the thermocautery. One can look for, and pin-point, the break by means of the diathermic electrode during the operation, with constant ophthalmoscopic checking. But it is none the less necessary to-day to hit the tear—that is, if we wish to achieve the 75%, 80% or even 85% of successful cures which now offer such a striking contrast to the one in a thousand cures that resulted from the treatments in use at the time of Vail's enquiry.

Now thirdly, what has become of Gonin's insistence that the retina must be brought as close as possible to the choroid before and during operation? It remains happily true that in cases of very recent detachment, rest for the patient and immobilization of the eye in the correct position are, almost always, enough to re-establish contact between the retina and the choroid and so to restore the visual field in a way that never ceases to impress the patient—so much so, that he begins to wonder whether the operation for which he is being prepared, cannot be avoided? And we can also confirm that the sooner and the more completely this contact is re-established the better is the operational prognosis.

The pre-operational evacuation of the sub-retinal fluid by scleral puncture has no lasting effect. Carried out at the beginning of the operation, it has the major disadvantage of inducing a state of hypotonia which makes the rest of the operation notably much more difficult.

Intravitreous injection, however, of air, saline or alien vitreous, given at the end of the operation, can help to keep the retina in place.

But what is to be done when the pre-operational re-establishment of contact between the retina and choroid (a concept as valid to-day as in the time of Gonin) cannot be achieved? It is said that when, on one occasion, a certain mountain declined to come to Mahomet, Mahomet decided to go to the mountain. So here, if the retina does not approach the ocular wall, the ocular wall must be encouraged to approach the retina. Thus "Mahomet's principle"—if I may so call it—has led to two approaches: the shortening of the sclera, and the buckling of the sclera.

Lindner—in 1931, when Gonin was still alive—was the first surgeon to shorten the eyeball by totally excising a segment of the sclera. He recommended the procedure in the following cases: (*a*) Aphakic eyes without detectable hole. (*b*) Aphakic eyes after unsuccessful operation. (*c*) Detachment with the retina fixed by strands. (*d*) Detachment operated upon several times without success.

Lindner's technique was first adopted in this country, as far as I know, by Juler and Lister, and by Seymour Philps.

In 1949, C. Dee Shapland conceived the idea of lamellar scleral resection and this is, of course, the method now favoured by most surgeons. Dee Shapland, from the start, indicated precisely which conditions he believed the method was likely to benefit: (*a*) Aphakic eyes. (*b*) High myopia. (*c*) Unsuccessful operations. (*d*) Large dialyses. (*e*) After perforating injuries.

In 1949 Weve recommended invagination (by means of firm sutures) of the intact section of the sclera which exactly corresponds with the tear; Arruga has recently advocated the circular tying-round of the eyeball—a last resort in almost desperate cases.

The shortening techniques have without doubt increased our operative possibilities, and enabled us to save—at least partially—many eyes that in the past would have been lost without hope. One can say the same of the buckling techniques, which aim at bringing the ocular wall and the retina together, as precisely as possible, in the exact site of the break.

Jess in 1937, with his pad of cotton-wool kept in place for two weeks, seems to have been the first to achieve this necessary bringing into contact of the choroid and the retina. Custodis with his Polyviol implant, Schepens with his polyethylene or Silastic tubes, and Dellaporta with his chromic catgut, have further endowed us with techniques which can improve the prognosis in difficult cases.

Fourthly, with regard to the pathogenesis of tearing and detachment of the retina, we have recalled how Gonin had built up a composite concept solidly based on his personal experience of anatomical pathology and his use of the ophthalmoscope: In his view, the choroid, the retina and the vitreous were all involved in a non-inflammatory degenerative process—a process which developed especially in myopic or aged eyes. Has our knowledge in this field made any great progress? It is very doubtful. We must rather recognize that the problem of the pathogenesis of retinal tearing is still basically unsolved, and this in spite of numerous contributions that have been made to its study.

According to Gonin, horseshoe tears (ruptures with flaps) are due to a tearing away of the retina at some point caused by some pathological adhesion of the vitreous. Pau recently offered the hypothesis that the adhesions were embryonic in nature.

Gonin, and Vogt after him, held that multiple retinal holes without flaps resulted from a cystic degeneration of the retina. Many authors recently have clarified the role of the small vessels, of sclerosis of the chorio-capillary layer and of perisclerosis of the terminal sections of the retinal arteries.

The general ætiology of the disease of the eye which culminates in retinal detachment is as obscure as it was twenty-five years ago, except that we now assign more importance to the hereditary factor.

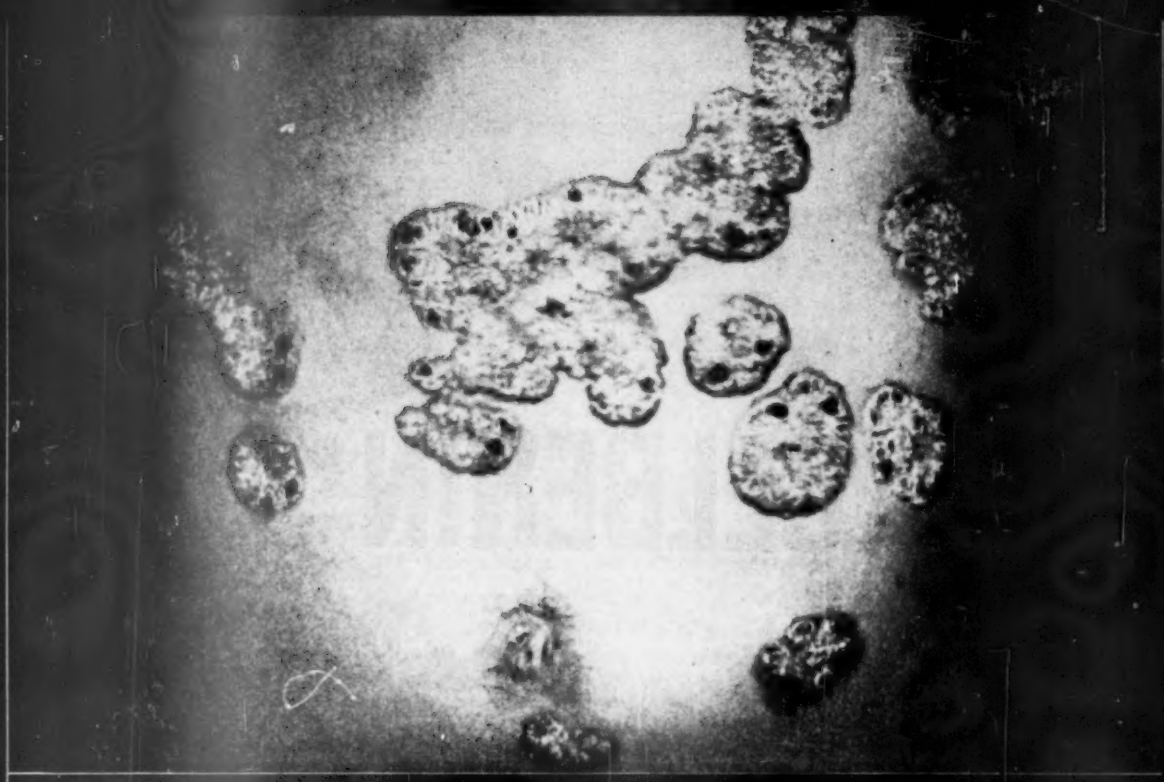
The hope that was so remote for my master Gonin has at last been realized by Meyer-Schwickerath, the hope of prophylactic intervention in cases of retinal tears discovered *before* detachment, and of areas of chorioretinal dystrophy or atrophy discovered *before* the formation of tears.

Photocoagulation has become the ideal method of prophylactic treatment, especially for the second eye of our patients. Indeed, whatever the fate of the first eye, we now must pay greater attention than we did in the past to the second eye, for there we often find suspicious peripheral areas of degeneration.

If Gonin took the first step, the decisive one, on the road that led to the successful treatment of a disease that, before his days, was incurable, we can say with justice that the second step has now been taken by Meyer-Schwickerath. For it is he who has enabled us to intervene earlier in the pathogenic chain than Gonin could, the links in this chain being degeneration, tearing and detachment.

From this historical survey we can conclude, I think, that the foundations laid by the master of Lausanne have held good because they were based on the labours of a man who was a sound scientific worker and a great doctor. His thought was penetrating while he himself was persevering and prudently audacious.

I have frequently in this paper referred to Gonin as "the Master". But if we think for one moment of the numerous eyes he saved from blindness, of the innumerable eyes saved from blindness since his death thanks to him, then a greater and perhaps nobler title may suggest itself to us: "Gonin, the servant."



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Section of Psychiatry

President—R. STRÖM-OLSEN, M.D.

Meeting June 14, 1960.

Diagnosis and Prognosis of Schizophrenia

By Professor GABRIEL LANGFELDT, M.D.

Oslo, Norway

THE diagnosis of schizophrenia differs from country to country, and even from hospital to hospital in the same country. It may be reserved for patients with a quite typical history, symptomatology and course; or become more comprehensive, to include psychoses with varied symptomatology and course.

Conditions were quite different before Bleuler in 1911 proposed the term schizophrenia to replace dementia præcox, thus extending the group to include psychoses of widely varying origin. Dementia præcox was precisely defined. For this reason it was relatively simple to compare the results of different treatments, and it was generally agreed that the prognosis of dementia præcox was very poor. Kraepelin (1910) reported that in his long-term study of dementia præcox 12·6% recovered immediately, only to relapse within two or three years, so that the number of lasting recoveries amounted to only 2·6%. At the same time 17% showed social remission, while the rest deteriorated. Although some disagreement existed as to the limits of Kraepelin's dementia præcox group, the possibility of deviating diagnoses was much smaller than after the acceptance of the term schizophrenia. But it was generally agreed that a lasting cure of dementia præcox was unusual. Most workers reported that 30–40% of the socialized group were more or less able to work, while the rest steadily deteriorated to a degree necessitating permanent hospitalization or other support.

There are notable differences in the reported results of dementia præcox and the *spontaneous* prognosis in schizophrenia, as defined by Bleuler —after 1911 the recovery rate ranges from 0–20% and the improved group is usually much larger than in dementia præcox. Further details are given by Bellak (1948); according to his statistics the amelioration rates range from 8·8 to 44%. There are two main reasons for these variations: first, the different delineation of the schizophrenia group—the more cases of genuine dementia præcox included the smaller the recovery rate; and secondly, the recovery and improvement rates depend on the type of schizophrenia and especially on the duration of the psychosis.

For many years I have attempted a more accurate diagnostic grouping of the schizophrenic picture (Langfeldt, 1926). By studying, among other things, the glucose tolerance, basal metabolism, blood picture, reaction to adrenaline, atropine and pilocarpine, in 40 cases of typical dementia præcox, I demonstrated that small deviations from the normal existed. These deviations, however, were not characteristic of any known endocrine disorder, but varied not only according to the duration (acute or chronic cases) and the phase of the disorder, but also according to the type (hebephrenic, catatonic, paranoid) of the schizophrenic psychosis. In some cases of catatonia there was a reduced basal metabolism which could not be raised by the administration of thyroid. In some cases, but not in all, there was insensitivity to intravenous injection of adrenaline. One of the principal conclusions was that the somatic findings differed in the different types of dementia præcox. The hypothesis was advanced that dementia præcox might be the result of a diencephalosis brought about by endocrine-vegetative imbalance. It is of paramount importance in psychiatric research to correlate the psychic syndrome with somatic findings when present.

In 1935 Sakel postulated that insulin-coma therapy could induce good social remission in 88% of schizophrenia as diagnosed at the Vienna Clinic. However, on examination of the patients' records it became apparent that many cases diagnosed as schizophrenia in Vienna would in Norway be grouped in other categories, e.g. psychogenic psychoses, reactive psychoses (psychoses in feeble-minded and psychopathic individuals), toxic or infective reaction types, and psychoses with organic brain disorders. I also noticed that while patients with such psychoses, which since 1937 I have grouped as *schizophreniform*, as a rule reacted favourably to the treatment, the cases which did not improve corresponded to the cases which at the Oslo Clinic were diagnosed as true schizophrenia. Stimulated by reports (Meduna, 1936) that cases which reacted favourably to Cardiazol treatment did not belong to the dementia præcox group (Kraepelin), I

decided to take 10 typical cases of schizophrenia and treat them with insulin coma using Sakel's method. 2 of them had a very short-lasting remission but relapsed, and all 10 had to be transferred to a mental hospital, although none had been ill more than one year. When followed up all had deteriorated severely. After this I was convinced that insulin coma could not effect real recovery in typical schizophrenia. Furthermore, I felt that cases diagnosed as schizophrenia which recovered or were much improved by the treatment, were those with a tendency to spontaneous remission and could be helped by less dangerous therapies. Insulin-coma therapy was therefore abandoned at the University Psychiatric Clinic of Oslo.

There was considerable interest in the spontaneous course of the psychoses diagnosed as schizophrenia (*see* Langfeldt, 1956), but most of the results were based only on written reports, often unreliable, from the patients themselves or their relatives. Comparison with the results of the follow up of individual cases showed that severely demented patients might well be reported as well adjusted (by being tolerated) and helping in the house. In 1936 I decided, in order to get reliable clues to the spontaneous course, to make fresh observations on 200 cases of schizophrenia which had been discharged from the clinic seven to ten years previously. From the opening of the clinic in 1926 an attempt had been made to group separately the cases considered as "true schizophrenias". If on discharge there was no doubt that the case belonged to this group the case was labelled only as *schizophrenia*, eventually with the *personality type* (schizoid, hysterical, paranoid, &c.) and *type of disorder* (hebephrenia, catatonia, paranoid) as subdiagnosis. In these cases possible other diagnoses were added, such as paranoid-hallucinatory psychosis in an alcoholic, sensitive self-reference, psychosis in a hypersensitive individual, confusional psychosis in a feeble-minded personality. My hypothesis was that those psychoses which were not considered as typical schizophrenias were those with a tendency to spontaneous remission, and which profited from insulin coma. I have suggested calling these conditions *schizophreniform psychoses* in contrast to the typical schizophrenias. 100 cases of schizophrenia assumed on discharge to belong to the typical group, and 100 doubtful (schizophreniform) cases which could be traced were followed up (Langfeldt, 1939). Tables I and II correlate diagnosis on discharge with diagnosis at follow up; the outcome is also correlated with the diagnoses. Between 1926 and 1929 when these patients were in hospital there was more disagreement over the concept of the central schizophrenia group than in 1936 when

TABLE I.—PROGNOSIS IN SCHIZOPHRENIA: FOLLOW-UP STUDY OF 100 TYPICAL CASES

	Cured	Improved	Unchanged or worse	Total
Diagnosis on discharge 1926–1929:				
Schizophrenia ..	17	17	66	100
Diagnosis at follow-up 1936:				
Typical schizophrenia	6	15	66	87
Schizophreniform psychosis ..	11	2	—	13

TABLE II.—PROGNOSIS IN SCHIZOPHRENIA: FOLLOW-UP OF 100 CASES DIAGNOSED AS ? SCHIZOPHRENIA

	Cured	Improved	Unchanged or worse	Total
Diagnosis on discharge 1926–1929:				
Schizophrenia? ..	32	25	43	100
Diagnosis on follow-up 1936:				
Typical schizophrenia	1	8	36	45
Schizophreniform psychosis ..	31	17	7	55

I made the catamnestic diagnosis. Consequently in the group originally classified as typical schizophrenia (Table I) 13 cases had not displayed the history and symptoms which, in 1936, met the diagnosis of true schizophrenia. From Table I it is seen that if we keep to the diagnoses on discharge the outcome is poor in that 66 of 100 cases were unchanged or worse, although 17 had completely recovered and 17 improved. If, however, we keep to the stricter concept of schizophrenia used in the follow up the outcome of the typical cases is still worse: of 87 cases considered at the follow up to be typical schizophrenia only 6 had recovered completely, while among the 13 cases grouped as schizophreniform psychoses 11 had made complete recoveries and 2 were improved. Similar results can be seen in Table II, representing the outcome of 100 cases in which a doubt had been raised at discharge whether they were typical schizophrenias: 32 had recovered, 25 improved, and 43 were unchanged or worse. By revision of the diagnoses, however, it appeared that of the 100 schizophreniform psychoses, 45 cases had a history and symptomatology which in 1936 was considered characteristic of the central group, and of these 45 only 1 had recovered and 8 improved. Of the 55 schizophreniform cases, 31 recovered and 17 improved, while only 7 were unchanged or worse. Thus by the diagnoses made at follow up, of 132 typical cases of schizophrenia 102 remained unchanged or were worse, while only 7 recovered and 23 were improved. Of the 68 schizophreniform psychoses only 7 were worse or unchanged while 42 recovered and 19 improved. These results indicate that by dividing the schizophrenia group into typical and schizophreniform cases we can differentiate between two groups with quite different prognoses, probably differing in ætiology and pathogenesis. Schizophreniform psychoses can as a rule easily be placed in other well-known groups of psychotic disorders, frequently with known ætiology, while

it is characteristic of the typical schizophrenias that the ætiology cannot be demonstrated.

Tables I and II deal with the spontaneous course of the disorders, submitted only to the type of hospital treatment usual at that time. For comparison with cases treated by electric shock, insulin coma and lobotomy Dr. L. Eitinger, Dr. C. Laane and I, in 1955, followed up 154 cases admitted to hospital during the years 1940–1949. There were in all 783 patients, 329 diagnosed as schizophrenia and 454 as schizophreniform states, of whom 154, those mentioned in this study, were re-examined individually by Dr. Eitinger and Dr. Laane. In this follow-up study I predicted the prognoses on the basis of the hospital records, while my colleagues made the actual re-examination of the patients. I therefore decided whether the case should be considered as one of typical schizophrenia; whether I expected the patient to recover, to improve or to remain unchanged. The prognosis, correlated with the outcome of the case five to fifteen years after discharge, is seen in Tables III and IV (Eitinger, 1959).

TABLE III.—PROGNOSIS IN SCHIZOPHRENIA: FOLLOW-UP RESULTS

	Typical schizophrenia	Schizophreniform	Prognosis +++	++	+	0	Total
Diagnosis from case records ..	110	0	0	2	11	97	110
Follow-up results	105	5	4	5	9	92	110

+++ = completely recovered.
++ = much improved.
\+ = slightly improved.
0 = no effect or worse.

TABLE IV.—PROGNOSIS IN SCHIZOPHRENIA: 44 CASES ASSUMED TO BE SCHIZOPHRENIFORM PSYCHOSES

	Typical schizophrenia	Schizophreniform	Prognosis +++	++	+	0	Total
Diagnosis from case records ..	0	44	10	23	6	5	44
Follow-up results	5	39	14	16	4	10	44

It is evident that in these cases, treated with electric shock, insulin coma or lobotomy, the outcome is much better in the schizophreniform cases than in the schizophrenias. The correspondence between prognoses and the actual outcome is surprisingly good: in 110 cases diagnosed as typical schizophrenia the diagnosis was confirmed in 105 cases; of the 110 cases only 4 had recovered and 5 improved; the remaining 101 being unchanged or worse. On the other hand, of 39 schizophreniform psychoses 14 were mostly unchanged, while 30 had recovered or were much improved. It seems that cases of typical schizophrenia treated with different therapies do not have, in the long run, a more favourable course than untreated cases (compare Tables I and II). In Tables V and VI the outcome of treatment in the two groups is summarized.

The treatments do not seem to have had any favourable influence on the typical cases, but in

TABLE V.—TYPICAL SCHIZOPHRENIA: RESULTS OF TREATMENT

Method	Results +++	++	+	0	No. of patients
E.C.T. only	0	4	5	45	54
E.C.T. and insulin coma ..	0	0	0	8	8
E.C.T. and lobotomy	0	0	0	22	22
E.C.T., insulin coma and lobotomy	0	0	0	1	1
No somatic therapy	1	0	3	16	20
				Total	105

TABLE VI.—SCHIZOPHRENIFORM STATES: RESULTS OF TREATMENT

Method	Results +++	++	+	0	No. of patients
E.C.T. only	12	12	1	4	29
E.C.T. and lobotomy	2	0	0	0	2
E.C.T., insulin coma and lobotomy	0	0	0	1	1
Lobotomy only	0	1	0	0	1
No special therapy	2	1	3	0	6
				Total	39

the schizophreniform cases it is possible that electric shock especially may have brought about a good remission. In my experience electric shock has been effective in many cases of schizophreniform psychosis, while it is of no help in cases of typical schizophrenia. For the last ten years we have not used electric shock in typical cases of schizophrenia.

As a result of more accurate diagnosis and follow-up investigations we are now able to diagnose the genuine schizophrenias, to differentiate them from schizophreniform cases, and to forecast the further development of these patients with a certainty of around 90–95%. It may of course be argued that it is not always satisfactory to base the diagnosis of a case on its probable outcome. It would certainly be better if the diagnosis could be based on knowledge of the ætiology and pathogenesis. However, despite more than sixty years of research in this field, almost nothing has been found which can be accepted as scientifically valid. One of the reasons for this is the excessive extension of the schizophrenia concept. It is unreasonable to expect to find common ætiological and pathogenetic factors in a group of psychoses with so many different manifestations. In other medical disciplines new ætiological and therapeutic discoveries have regularly been made by isolating from large groups smaller ones with something in common in symptomatology and outcome. In psychiatry general paresis, formerly grouped with the neuroses, is an example of the importance of more accurate diagnosis based on both psychic and somatic symptoms. It was accurate diagnosis, too, which helped Gjessing (1932) to differentiate the circular catatonias from the ordinary cases of catatonia. For this reason I am much in favour of a more refined diagnostic technique in in the schizophrenias. It is most important with these patients to diagnose true schizophrenia only

when positive and fundamental symptoms are demonstrable, and to group all other schizophrenia-like cases as schizophreniform psychoses. But in these two large groups a further differentiation should take place based on the psychic syndromes and when present the somatic findings.

The interest in a dichotomy of the schizophrenia group seems to be increasing. At the 2nd International Congress of Psychiatry the schizophreniform psychoses were placed as a special topic, and several research workers showed the prognosis of cases in this group to be different from that of genuine schizophrenia. In a recent monograph by Hallgren and Sjögren (1959) the very poor prognosis of the central schizophrenia group, diagnosed according to my criteria, has been convincingly demonstrated in connexion with a census investigation in a rural Swedish population. All cases which could be traced (88% of the material) were shown at follow up to have deteriorated.

What, then, are the clues to the diagnosis of schizophrenia, by which the prognosis can be indicated with a certainty of 90–95%? A comprehensive reference is made in my book (1956) to the experience of other workers; here I shall stress only the following: neither hereditary conditions, personality nor bodily types are of any help in the diagnosis of genuine schizophrenia. Psychological and biological tests have not up till now been of decisive help, nor are there any diagnostically significant somatic findings. Acute onset and exogenous precipitating factors have been considered by many authors as prognostically favourable. Among my cases are many with an acute onset which have run a very unfavourable course, and even cases which seem to have been exogenically precipitated may deteriorate and result in typical schizophrenic dementia. The best clues to the diagnosis of the genuine type of schizophrenia with poor prognosis are in my experience the initial changes in the personality and the mental symptomatology. The personality changes characteristic of many typical cases of schizophrenia manifest as a special type of emotional blunting followed by lack of initiative and altered, frequently peculiar, behaviour. In hebephrenia especially, these changes are very characteristic and a principal clue to the diagnosis. The changes are frequently more difficult to describe than to apprehend, but the experienced psychiatrist regularly feels intuitively that he is confronted with a morbid personality of the genuine schizophrenic type. In catatonic types the history as well as the typical signs in the periods of restlessness and stupor (negativism, catalepsy, vegetative symptoms, &c.) are frequently so characteristic that no doubt can exist that the case is typical schizophrenia. The greatest difficulty arises in connexion with paranoid cases of schizophrenia. In many places in Europe and the U.S.A. all types of paranoid reactions are diagnosed as schizophrenia, especially if the patients are also hallucinated. This is an unfortunate trend in international psychiatry; paranoid ideas and hallucinations are symptoms which can occur in all types of psychotic reactions and can as such give no clue to the diagnosis of true schizophrenia. Our follow-up investigations showed two syndromes with paranoid symptoms which are regularly associated with a poor prognosis, viz. cases characterized by the essential symptoms of splitting of the personality (depersonalization symptoms[1]) and the loss of reality-feeling (derealization symptoms[1]), and the group described by Kraepelin (1910) as dementia paranoides, characterized by primary (in contrast to secondary) delusions. In my experience depersonalization and derealization symptoms occur mostly in younger schizophrenics, while dementia paranoides seldom starts before the age of 40. In addition to these two syndromes chronic hallucinations are also indicative of schizophrenia if organic brain disorder, infections and intoxications can be excluded. I cannot here describe in detail the symptoms characteristic of the depersonalization and derealization states, but to be sure of the diagnosis of true schizophrenia it is not enough that the patient talks about being influenced by forces from outside himself or that his surroundings are changed; he must also *experience* these influences and changes. Mild depersonalization and derealization symptoms may occur transiently in other psychoses and in neuroses, and especially in confusional states. A period of two to three weeks' observation is sometimes necessary to exclude special ætiological factors, more particularly organic brain disorder and intoxications. However, if no signs of the latter can be demonstrated, a psychic picture dominated by depersonalization and derealization is very characteristic of true schizophrenia associated with a very poor prognosis. Occasionally the premorbid changes of

[1]The terms *depersonalization* and *derealization* are here given a special meaning. Although they are frequently used in connexion with psychasthenia, hysteria, obsessive-compulsive and other neurotic conditions, in this paper they signify syndromes characterized by experiences of a special type of disturbance of volition and the self, called "Ichstörungen" by Meyer (1959), and found usually only in schizophrenia. The principal differentiating signs are that the schizophrenic patient has no insight into his own condition and that he always experiences the disturbances as originating outside himself. These syndromes manifest for instance as passivity feelings, associated with ideas of reference affecting the psyche (thoughts, emotions and actions), or body (physical influence delirium).

TABLE VII.—429 CASES OF NEUROSES AND PSYCHOSES TREATED WITH ELECTRO-SHOCK 1942–1944: FOLLOW UP AFTER ONE YEAR

Predominant Mental Traits	Influence-phenomena	Chronic hallucinations	Primary delusions	Secondary delusions	Manic hypomanic traits	Depressive traits	Melancholiform traits
Cured	4	1	1	2	3	32	36
Improved ++	5	1	0	11	8	57	40
Improved +	10	4	4	12	5	108	21
Unchanged or worse	49	18	16	10	5	46	14
Total	68	24	21	35	21	243	111

personality may help to determine the diagnosis, but the symptoms mentioned are essential and usually pathognomonic. The same may be said of the primary delusions and chronic hallucinations which characterize many cases of typical schizophrenia. I feel that these symptoms are manifestations correlated to the primary cause or causes of true schizophrenia. Firstly, these symptoms do not seem to be psychogenically understandable and it is, therefore, more reasonable to assume that they are the product of a primary pathophysiological or neuropathological disorder influencing the functions of the brain. Secondly, it seems that the influence-phenomena and other signs of depersonalization as well as primary delusions and chronic hallucinations (*see* Table VII) are associated with an unfavourable prognosis. In Table VII the effect of electro-shock treatment in 429 cases of different neuroses and psychoses is demonstrated. Cases with influence-phenomena, chronic hallucinations and primary delusions are associated with a very poor outcome, and these symptoms thus usually indicate a poor prognosis. Most of these cases were diagnosed as schizophrenias, the follow up being done by Dr. P. Anchersen.

In conclusion I wish to stress the following diagnostic signs and symptoms of true schizophrenia: (1) A break up in the development of a personality. (2) Catatonic stupor or excitement. (3) Symptoms of depersonalization and derealization. (4) Primary delusions as seen in paranoid cases.

Concerning the symptomatology of schizophreniform cases several authors (Table VIII)

TABLE VIII.—SCHIZOPHRENIFORM PSYCHOSES (LANGFELDT)

Cloudy states:	Bleuler: Twilight states.
	Mayer-Gross: Oneiroid states.
	Meduna: Oneirophrenia.
Emotional states:	Claude: Schizo-mania.
	Kleist: Cycloid psychoses.
	Leonhard: Atypical schizophrenias.
	Schizo-affective states.
	Pseudoneurotic schizophrenias.

Otherwise many constitutional, psychogenic and brain-organic conditioned psychoses manifest themselves by a schizophreniform picture.

have described psychoses to which they have given different names because they deviate symptomatically from the genuine schizophrenias; these are usually confusional (cloudy) or emotionally abnormal states, and paranoid states. Many psychoses in feeble-minded, hysterical, obsessional, paranoid and hypersensitive individuals are characterized by delusions and hallucinations, but lack the other symptoms of true schizophrenia. The reason why these cases are often mistaken for schizophrenias is probably that the personality types contribute to the symptomatology some features, e.g. schizoid traits, emotional flattening, ideas of reference, which can resemble genuine schizophrenic symptoms However, the further course of these cases is much more favourable than that of true schizophrenia. Catamnestically it has also been possible, as a rule, to group the schizophreniform cases into categories with more or less known ætiological or pathogenic factors.

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DISCUSSION

Dr. Ian Skottowe (Oxford) believed that the introduction of the term schizophrenia some fifty years ago, though socially desirable in tending to lead away from previous fatalistic conceptions, had come to have certain disadvantages. It had tended to produce a certain woolliness of thought and in some ways it might even hinder fundamental researches because its clinical criteria were not applied stringently enough. This weakness might be enhanced if schizophrenia continued to be a diagnosis by exclusion—all psychoses in young people that were not clearly manic-depressive nor symptomatic of organic brain disease or gross toxæmia. Professor Langfeldt had shown courage in continuing to use the term dementia præcox up till 1926, at least; and since then he had done considerable service to psychiatry by distinguishing a nuclear, or "central", group of patients within the congeries of schizophrenic illnesses. To reserve the term schizophrenia for this central group

and to designate other cases, superficially similar, as schizophreniform states (though Dr. Skottowe would prefer "schizophrenoid") was helpful to research. He agreed with Professor Langfeldt that many of these other cases turned out to be personality reaction-types, toxic states, dream-like states, or, with more severe symptomatology, atypical depressions in which hallucinations or paranoid trends happened to be prominent. The outcome of most of them was favourable, whereas the outcome in "nuclear" schizophrenia remained, in general, much less good. But a distinction should not rest on outcome alone. The finer points of clinical diagnosis should enable us to distinguish one group from the other at an early stage.

Professor Langfeldt had said in effect that constant symptoms might be expected to march with, or reflect, a constant pathology. Since, with the exception of the small group of periodic catatonias (Gjessing's syndrome), there was very little positive knowledge of any somatic pathology in schizophrenia, it was desirable to continue to try to group together cases with constant clinical symptoms. If such a group were then scrutinized in the various disciplines concerned in research, a constant pathology might ultimately be found.

While having due regard to individual differences among patients, occasioned by their life-experiences and circumstances, essential similarities among them should still be sought; and these similarities would constitute the criteria for inclusion in the truly schizophrenic group.

In the course of an interim review of a continuing survey of mental hospital admissions over several years, which Dr. Skottowe was undertaking with Dr. R. W. Parnell[1], it had been decided to take as the symptomatic criteria for schizophrenia: (1) Disorder of the thinking process, and (2) incongruity of mood. It was a requirement that these phenomena should occur in a clear sensorial setting. The presence of delusions and hallucinations was not essential, but if they were prominent the case was designated paranoid schizophrenia, provided that the disordered thinking process and incongruity of mood could also be discerned.

When these criteria were applied strictly, the proportion of patients diagnosed as schizophrenic among all patients admitted shrank remarkably as was shown in Table I.

Dr. Skottowe accepted Professor Langfeldt's finding that the diagnosis of schizophrenia differed from

TABLE I.

Sample	Extent to which schizophrenia was diagnosed in all patients admitted below the age of 65
England and Wales (1953)	28%
Oxford Region only	21%
Parnell and Skottowe's survey: (four out of five hospitals in the Oxford Region)	13%

[1]PARNELL, R. W., and SKOTTOWE, I. (1959) *Brit. med. J.*, ii, 1296.

hospital to hospital. To agree upon stringent diagnostic criteria was essential. Confusion might follow if "depersonalization" and "derealization" were given meanings different from the usual.

What were the other cases that had been diagnosed as schizophrenic—the balance between the 13% and the 28% in Table I? He could not tell at this stage. Many of them would no doubt be regarded by Professor Langfeldt as schizophreniform (or schizophrenoid) states. But some might turn out to be of the same nature as nuclear schizophrenia, though they had not been discerned at an early stage because of relatively unrefined clinical methods. That, however, did not, invalidate the delineation of a nuclear group by constant positive findings, certainly for research purposes. There was a high concordance of diagnosis by different observers dealing with the same cases in the nuclear group that the survey revealed—as there was in Professor Langfeldt's surveys.

Professor E. Stengel (Sheffield) said that Professor Langfeldt's proposal to restrict the diagnosis of schizophrenia to patients with a bad prognosis was a valuable working hypothesis. His prognostic criteria deserved to be carefully tested. His "real" schizophrenia appeared to correspond to the nuclear group of other authors. Professor Langfeldt's approach was in keeping with a recent trend towards a return to the early Kræpelinian entity of dementia præcox. Whether the nuclear group presented the real or true schizophrenia was not known. Obviously, this concept of schizophrenia differed fundamentally from that of Bleuler which allowed for far-reaching remissions and even recoveries. Patients diagnosed according to Bleuler could not therefore be compared with Langfeldt's schizophrenics. Skottowe's diagnostic criteria were less restrictive than Langfeldt's but more so than Bleuler's. Other psychiatrists used other concepts, often without being aware of it. These differences of diagnostic criteria were responsible for a great deal of confusion which made comparison of clinical data impossible. Even if individual authors defined their use of the term schizophrenia, as Professor Langfeldt had done, there would always be a tendency to assume that the same word meant the same thing to all of them. That was why Professor Langfeldt's use of the old-established terms depersonalization and derealization was bound to lead to misunderstandings, even though he had redefined them. In a recent report to the World Health Organization about the present state of psychiatric classification Professor Stengel had proposed the adoption of operational definitions for the purpose of an international classification of mental disorders (*Proc. R. Soc. Med.*, 1960, **53**, 123). Psychiatrists badly needed such a tool of communication. They must get away from the idea that, at the present state of knowledge, terms such as schizophrenia stood for well-defined biological realities. They were, in fact, no more than hypothetical concepts.

These comments on some semantic aspects of Professor Langfeldt's presentation should in no way detract from the great theoretical and practical importance of his clinical observations.

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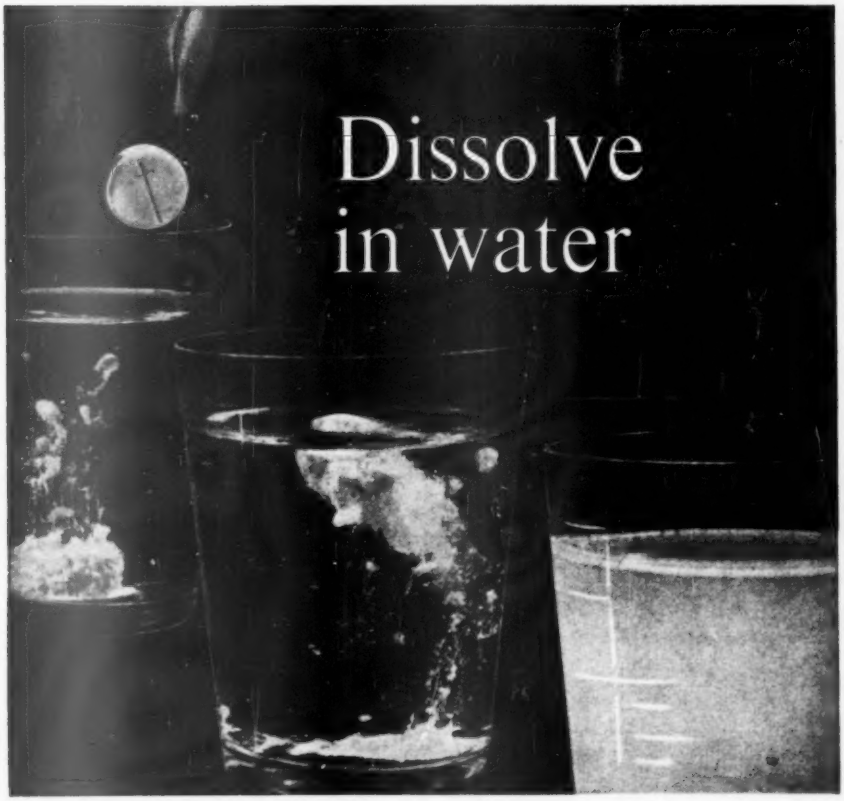

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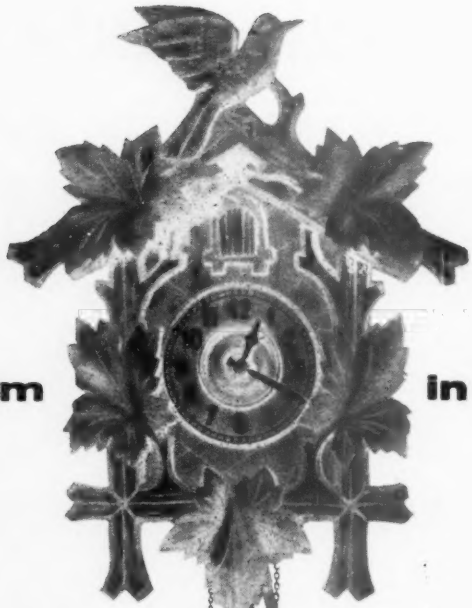

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PAPERS

The Peutz-Jeghers Syndrome [*Abridged*]

By D. B. E. FOSTER, F.R.C.S.
Cardiff

THE Peutz-Jeghers syndrome consists of familial polyposis of the gastro-intestinal tract, associated with pigmentation of the buccal mucosa, the face and other parts of the skin. This condition, once seen, can be diagnosed by simple observation. It has only been generally recognized for the past eight to ten years, though by 1957 Bartholomew *et al.* were able to record 75 cases of the syndrome.

It is interesting to note that it is probably as common as familial polyposis of the colon. This represents approximately 15 new cases of the syndrome being born to healthy parents in Great Britain annually (Dormandy, 1958). It is a condition which should be recognized because treatment is of such importance.

In 1896 Sir Jonathan Hutchinson first described twin girls in whom he had noted extensive pigmentation around the mouth and nares, but he did not pay more attention to it than that. In 1919 Parkes Weber recorded that one of the twins had died eleven years later following an operation for intussusception. Two years later Peutz of the Hague recorded his famous family in which he was able to collect 7 proven cases of the syndrome extending over 3 generations.

In 1949, Jeghers and his colleagues reported a further 10 cases, and made an extensive review of the literature. In this country Tanner (1951) reported to the Dermatological Section of this Society a family who showed gastric and jejunal polyposis associated with pigmentation.

My own interest in this condition arose in 1944 when I recorded (Foster, 1944) 2 cases of polypi with intussusception occurring in father and daughter, both patients exhibiting oral pigmentation. At that time I was not aware of the syndrome described by Peutz. This family was carefully studied and a further member aged 11 years presented with pigmentation and abdominal pain, but no definite polypi were found on investigation and laparotomy was not considered justifiable. However, thirteen years later this patient presented with acute symptoms, and was operated upon for intussusception due to an intestinal polyp of typical Peutz type.

More recently, a young girl of 12 years has been under my care. She had first presented with rectal bleeding, but the syndrome was recognized and she has been shown to have gastric, intestinal and colonic polypi. There is, however, no family history obtainable.

The polyps are predominantly in the small intestine. They rarely occur in the stomach or colon.

It is important to note that periodicity of growth of the polypi is common and there may be long quiescent periods. Thus any attempt at total ablation of the polypi at any one time will fail.

The polyps are composed of well-differentiated epithelia covering smooth muscle. Some irregularity of acinar cells may be present, and this together with the apparent invasion of the deeper layers probably accounts for the reported malignant change which has been recorded in these cases.

Reports from the Mayo Clinic (Bartholomew *et al.*, 1957) and the views of Morson (1958) suggest that these polypi are not neoplastic, but are more in the nature of a congenital abnormality or hamartoma. If this is the case, then they are not precancerous. I do not think there is at present sufficient evidence for regarding Peutz-Jeghers polyps as precancerous.

The syndrome is inherited through a mendelian dominant gene and the offspring of those with the disease have a 50% chance of being affected. The clinical picture is interesting and can be very confusing. The story is one of repeated intussusceptions which are usually transient, obstruct rarely and strangulate exceptionally. Attacks of colicky pain with the patient frequently feeling a vague lump are the main complaints.

Self-induced vomiting, postural changes or abdominal pressure may quickly abort the attacks of pain. Little wonder therefore that many of these patients have been labelled as hysterics. Rectal bleeding is an uncommon feature.

Pigmentation consists of tiny dark brown or black macules grouped predominantly around the mouth, nostrils and eyes. They are not hairy or vascular and may vary in number from a few to several hundred. The degree of pigmentation bears no relationship to the severity of the intestinal symptoms. Pigmentation may occur towards the bases of the nails and on the palms and there is a tendency for the fingers to be clubbed. Beginning at birth or in infancy the pigmentation fades towards puberty. It must be emphasized, however, that the buccal lesions remain unchanged and this site of pigmentation, often fainter than on the face, is a *sine qua non* of the diagnosis. Associated abnormalities such as adenoma of the bronchus, adenomata of the bladder and ovarian cysts may be present. The diagnosis is self-evident and investigations are not essential. Occasionally barium studies will show extensive gastric and intestinal polypi, whilst barium enema studies or sigmoidoscopy may reveal colonic polypi.

Acute cases usually present with intussusception which frequently resolves spontaneously and only rarely requires urgent intervention. In the chronic case, conservatism must be the watchword. In view of the tendency to bursts of spontaneous growth of the polypi no permanent cure can be assured even if all the polyps present at one time are removed and operation therefore should be avoided if possible. This policy is I believe safe in view of the present conception of the underlying nature of the lesions. Should surgical intervention become necessary the emphasis must be on conservative methods and extensive resections are to be condemned.

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The following papers were also read:

Mammary Mutations.—Dr. J. JACOBS. The paper referred to many physical abnormalities in the breasts which tended to increase the mental anxiety in the mother. A series of slides was shown of these abnormalities.

Troublesome Tracheo-œsophageal Fistulæ.—Mr. DILLWYN THOMAS.

Some Sleep Problems in Children.—Dr. P. T. BRAY.

DEMONSTRATIONS

The Handicapped University Student.—G. GRANT, M.B.

The development of special university health services has enabled the extent and nature of illness and disability among students to be investigated, and morbidity studies have shown that disorders of a "chronic or continued" nature may be responsible for as much as 40% of the total sickness experienced during a given period (Grant, 1957). The purpose of this communication is to illustrate—against a background of general morbidity—how the seriously handicapped student may make a success of a university career and to discuss some of the problems involved.

Table I gives the prevalence of certain chronic disorders among a group of some 2,008 students attending a Welsh College during a single academic year. Not all the conditions enumerated were the cause of serious handicaps, but experience in the University of Wales as a whole during the past twelve years suggests that, provided there is reasonable certainty about academic ability, quite severe physical and even psychological defects need not necessarily prove a bar to university education. For example:

Case I.—A male student, partially-sighted as the result of interstitial keratitis at the age of 11, whose entry to university was delayed by the development of respiratory tuberculosis, obtained an Honours degree in three years.

Case II.—A woman student had a pneumonectomy at the age of 9 for bronchiectasis. The remaining lung was diseased. No formal education was received until the age of 16. She entered university at 22 years of age and after obtaining an Honours degree in three years, successfully completed a Social Science course.

Case III.—An overseas student was found to be suffering from cerebral cysticercosis but obtained a Pass degree in four years despite major epileptic attacks.

Case IV.—A student with Morquio's disease entered university at the age of 19 having made normal educational progress and is managing a degree course in engineering satisfactorily despite occasional absences with respiratory infection.

Cases V and VI.—Among those with orthopædic disabilities one student with congenital absence of both femora and another with congenital absence of hands and feet have managed university courses.

TABLE I.—MORBIDITY AMONG 2,008 STUDENTS DURING THE ACADEMIC YEAR 1958–1959. PREVALENCE RATES PER 1,000 STUDENTS—SELECTED CHRONIC (LONG-TERM) CONDITIONS

Based on attendances at the Student Health Service, Student Health Service Records and Medical Certificates accounting for absence supplied by General Practitioners (the conditions did not necessarily commence during the period under review)

Condition	Males		Females		Total	
	No.	Rate per 1,000	No.	Rate per 1,000	No.	Rate per 1,000
Serious Psychological Disorders:						
Including 11 previously in hospital and 5 admitted during the year*	37	27·0	18	28·3	55	27·5
Ear, Nose and Throat:						
Relapsing otitis media, sinusitis, deafness, &c.	37	27·0	6	9·4	43	21·4
Skin Diseases:						
Psoriasis, eczema, severe acne, &c.	26	19·0	7	11·0	33	16·4
Orthopædic:						
Old poliomyelitis, congenital disorders, &c.	21	15·3	8	12·6	29	14·4
Sequelæ of injury	10	7·2	1	1·2	11	5·4
Medical:						
Asthma	25	18·2	8	12·6	33	16·4
Respiratory tuberculosis (3 new cases, 2 receiving ambulant therapy, and 9 under supervision)	11	8·0	3	4·7	14	7·0
Peptic ulcer (5 new cases)	14	10·2	—	—	14	6·9
Diabetes mellitus (1 new case)	6	4·4	—	—	6	2·9
Epilepsy (idiopathic 2 new cases)	5	3·6	—	—	5	2·5
Rheumatic heart disease	3	2·2	2	3·1	5	2·5
Congenital heart disorder	2	1·5	1	1·6	3	1·5
Bronchiectasis	2	1·5	4	6·3	6	2·9
Others—including loaiasis (1), congenital spasticity (2), nypertension, obesity, &c.	12	8·7	16	25·1	28	13·9
Surgical:						
Cerebral tumour (1), malignant melanoma (1), abdominal tuberculosis (1), renal calculus, hæmorrhoids, hernia, hydrocele, &c.	19	13·8	3	4·8	22	11·0
Gynæcological (severe)	—	—	15	23·5	15	7·0

* In addition approximately 10% attended with less severe psychological disturbances. There were 37 hospital admissions for chronic disorders during the year.

Sometimes handicapped students enter the university with fixed ideas about their future careers and it is important to encourage them to think along sensible lines from the outset, rather than to wait until after graduation only to find they are debarred on medical grounds from the career or profession of their choice. Guidance about courses of study and careers is given in the light of the medical history and in this and in eventual placement (which in most cases has not proved especially difficult) the co-operation of college careers advisers and of the University Appointments Board is invaluable.

Accommodation may also present acute problems for the disabled student and the help of supervisors of accommodation is invariably required. It is, for example, important to ensure that a student with a history of respiratory tuberculosis is not housed in lodgings where there are children. Those with disorders of locomotion (e.g. old poliomyelitis, spastics, &c.) may be presented with special difficulties and have, in a number of instances, had to learn to use a motorized invalid carriage during their first few months at the university. Special ramps may have to be constructed about college buildings. It is important to obtain prior information about handicaps of this kind. The student can then be invited, with the parents if possible, to visit the prospective college and estimate precisely the difficulties to be encountered in getting about from one department to another. Parents are, not unnaturally, occasionally somewhat overprotective, and need to be reassured.

It says much for these young men and women that they should have embarked on what is, for many, a difficult venture. They deserve every encouragement. It follows that handicapped children—and their parents—should not be discouraged from attempting to make the most of intellectual capabilities.

REFERENCE

GRANT, G. (1957) *Roy. Soc. Hlth J.*, **77**, 419.

The Natural History of Spina Bifida Cystica.—K. M. LAURENCE, M.B.

This investigation was based on 407 cases of spina bifida cystica seen by members of the staff of The Hospital for Sick Children, Great Ormond Street, and the Westminster Children's Hospital between 1947 and 1956. Of these only 38 cases were true meningoceles and all the remainder were regarded as myeloceles. All the patients were followed up and the survivors re-examined.

The pattern of disability was largely dependent upon the position of the spinal lesions. The percentage of cases with limb involvement was greatest in those with the sac in the lumbar region, while those with the upper dorsal and lower sacral lesions less frequently showed severe paralysis. On the other hand the lower the sac along the cerebrospinal axis the more frequent was the occurrence of sphincter paralysis. The incidence of hydrocephalus, which was present in at least 62% of the whole series, also varied according to the site of the sac. 80 and 70% of the lumbar and dorsilumbar but only 50 and 43% of the purely sacral and upper dorsal sacs, respectively, had associated hydrocephalus. This hydrocephalus was often present at birth or became manifest soon after. All too frequently, however, it developed later, but almost always before six months, usually as a result of ascending meningitis.

The survival rate in the series was 55%, and amongst these were all the meningoceles. This

figure is, however, misleading, as it takes no account of the patients actually at risk. According to a "life-table" as used by Insurance Actuaries the life expectancy is 36% to the age of 12 years or over in the whole series and 24% in the lumbar myeloceles, the largest single group.

Most of the deaths occurred in the first year of life, usually from intracranial infection (86 cases). The majority of the later deaths were due to hydrocephalus (49 cases) and renal failure (10 cases). Some died suddenly following investigation (5 cases). Although hydrocephalus was not the commonest immediate cause of death, 172 of the 185 patients who died suffered from hydrocephalus and 75% of those with obvious hydrocephalus have not survived.

It was concluded that: (1) only 10% of the cases were meningoceles; (2) one-third of all the cases survived twelve years or more; (3) clinical features were largely dependent upon the site of the lesions; (4) although intracranial infection was the commonest cause of death, the development of hydrocephalus was a grave prognostic sign as few of these cases survived.

It was suggested that if results are to be improved the raw spinal lesions should be covered by skin grafts as a surgical emergency on the first day of life to reduce the destruction of any functioning cord tissue of the myelocele and to avoid ascending infection.

Hydatid Disease in South Wales.—L. R. WEST, M.B.

Hydatid disease has almost entirely disappeared in Great Britain, except for a small area of South Wales where human cases are still encountered. While some 150 cases of the disease have been admitted to South Wales hospitals in the last ten years, and the maximum number of the 25 cases was seen in 1957, in the last three years there has been a sharp decline. The number of children found infected, which probably reflects the current prevalence of hydatidosis in any district, has fallen to one case a year.

In this series the liver alone was involved in 44% of cases, the lungs alone in 43%, both organs in 6%, and cysts occurred in other sites in 7%. The mortality of 9% indicates the dangers of complicated cysts and the difficulties of the surgery of hepatic cysts.

There is no evidence that any animal other than the sheep and domestic dog is implicated in the perpetuation of the life cycle of the parasite *Echinococcus granulosus* in South Wales.

The extent of ovine infection can be arrived at from examination of carcasses at slaughter yards which draw a substantial number of animals from known areas in Wales. Thus 0·9% of sheep at Cardiff abattoir are found infected, while a recent survey at two large English metropolitan abattoirs revealed infection rates of 2·7% and 5·6% among Welsh flocks. Districts of high infection rates are found near Brecon, Abergavenny, Usk, Monmouth, Builth Wells, and in several areas of Glamorgan. The extent of infection among sheep does not appear to have declined since Wolfe reported a 0·5% rate in 1943.

The extent of canine infection is difficult to measure. The minute parasite can be positively identified only by careful post-mortem examination of the mucous membrane of the gut near the jejuno-ileal junction. In a random sample of 50 house dogs drawn from Cardiff, Pontypridd and Merthyr Tydfil the author found 4 infected animals. Sheep-dogs were excluded from this sample.

The perpetuation of the life cycle of the parasite depends upon the dog gaining access to the viscera, particularly the liver, of the infected intermediate host, the sheep. In the modern abattoir, this possibility has been eliminated, but the same cannot be said for the knacker's yard. Under the primitive conditions of home slaughtering, still practised on outlying farms, the offal is customarily thrown to the dog. The use of offal as fertilizer by the market gardener offers another loophole since when buried in a shallow trench it is easily recovered by the dog, and under these conditions hydatid cysts remain fertile for seven days. The unfenced mountain pastures of South Wales also offer an ideal hunting ground for canine predators, which account for up to 1,000 reported killings annually.

The extent of human infection in South Wales does not constitute a public health problem, nor would measures designed to eradicate the disease be practicable, involving as they would changes in animal husbandry practices and a reduction both of the numbers and the liberties of the ubiquitous dog. Nevertheless it can safely be assumed that while a substantial animal reservoir of the disease persists, human cases will continue to be encountered.

REFERENCE

WOLFE, H. R. I. (1943) *Lancet*, i, 795.

The following demonstrations were also given:

Radiology of the Upper Gastro-intestinal Tract.—Dr. GRAHAM HINDE.

Prophylactic Antibiotics in Asthma.—Dr. WILLIAM DAVIES.

Paper Mounted Sections of Organs.—Professor J. GOUGH.

Unusual Congenital Heart Anomalies.—Dr. R. SEAL and Dr. K. M. LAURENCE.

Diagnostic Classification Index.—Professor A. G. WATKINS and Dr. O. P. GRAY.

The Effect on the Fœtus of Maternal Drug Therapy.—Professor A. S. DUNCAN.

Factors Related to the Neonatal Death Rate and Stillbirth Rate in the City of Cardiff in 1956.—Dr. MARIE RICHARDS.

Thrush.—Dr. J. JACOBS and Dr. JILL BRYANT.

A Dye Test for Tissue Injury.—Mr. EMLYN LEWIS.

(1) Tumours of the Urinary Tract in Childhood. (2) Diphallus with Vesica Duplex and Rectal Agenesis.—Mr. R. A. MOGG.

(1) Perinatal Mortality. (2) Chromatography.—Dr. T. E. PARRY.

Practical Problems of Pædiatric Anæsthesia.—Dr. BARBARA ROBERTS and Dr. P. W. THOMPSON.

Pollen Grains and Fungus Spores as Allergens.—Dr. H. A. HYDE and Dr. D. A. WILLIAMS.

Heart Models.—Dr. J. D. SPILLANE.

CASES

Cyclical Neutropenia.—P. T. BRAY, M.R.C.P.

The patient, a 9-year-old girl, had been subject to recurrent skin and respiratory infections since infancy. At the age of 18 months she had been seen in the Dermatology Clinic, where a diagnosis of necrotizing furunculosis, due to penicillin- and streptomycin-resistant staphylococcus, was made.

Following tonsillectomy at the age of 4½ years, there was severe infection in the tonsil beds, with secondary hæmorrhage and phlegmonous cervical adenitis.

In December 1956 she had a troublesome nasal furuncle followed by an abscess in the right labium majus. Two weeks later she became seriously ill with fever (temperature 104° F), vomiting, delirium, cough and dyspnœa. *Examination on admission* to hospital showed "typhoidal state", multiple cutaneous abscesses, jaundice with an enlarged and tender liver, albuminuria, and signs of bronchopneumonia.

Investigations.—Chest X-ray: Widespread circular opacities, many with clear central areas.

Blood culture: *Staph. pyogenes*, resistant to penicillin, streptomycin and tetracyclines; sensitive to chloramphenicol and erythromycin.

The pulmonary lesions were considered to be disseminated (hæmatogenous) staphylococcal pneumonia.

Liver function tests: Alkaline phosphatase 21 units, thymol turbidity 3 units, colloidal gold ++++, serum bilirubin 2·7 mg/100 ml.

Plasma proteins: Albumin 2·65, alpha-1 globulin 0·75, Alpha-2 globulin 1·32, beta globulin 0·94, gamma globulin 2·08 g/100 ml.

Urine: Albumin—cloud. R.B.Cs ++. Bilirubin present. Urobilinogen increased.

Blood count: Hb 12 g%. W.B.C. 6,000 (polys. 12%, lymphos, 55%, monos. 33%).

Bone marrow: Cellular marrow, normal erythropoiesis, but metamyelocyte maturation arrest.

Treatment.—Intravenous fluids with chloramphenicol. Intramuscular erythromycin.

Progress.—From the day after admission, the jaundice deepened for several days, the liver becoming further enlarged. Coarse crepitations persisted throughout the lung fields, and the general toxæmic state continued until the fourth day.

For the next seven weeks a relapsing intermittent fever continued, with wide variations in the total and differential leucocyte counts. The total white blood count ranged from 1,500 (3% polys.) to 15,000 (20% polys., 30% metamyelos).

Chloramphenicol was stopped after fourteen days (total given = 7 g). Erythromycin was continued alone for a further two weeks, followed by novobiocin and oleandomycin for three weeks.

A tender indurated swelling in the left posterior axillary region developed, and eventually 200 ml of thick sterile pus was aspirated from it. X-rays showed osteolytic areas in the scapula.

Subsequent admissions because of infections were as follows: April 1957 (aged 6 years): Left mastoiditis; cortical mastoidectomy performed; pus grew *Staph. pyogenes*. November 1957: Large left inguinal abscess; on culture—beta hæmolytic streptococcus. November 1958: Gluteal abscess: *Staph. pyogenes*. June 1959: Axillary abscess: *Staph. pyogenes*. July 1959: Right inguinal abscess: *Staph. pyogenes*. October 1959: Cervical abscess: sterile.

Apart from these infections necessitating admission, recurrent furuncles and infected abrasions were numerous. Severe neutropenia, at intervals of approximately twenty-one days, was regularly noted in the serial blood counts done during this time. The polymorphonuclear count was seldom above 750 per c.mm, for more than a day or two.

Treatment with ACTH, steroids, folic acid, vitamin B_{12}, all seemed to be without effect on either the clinical state or the blood picture.

Tracheomalacia.—O. P. GRAY, M.R.C.P.

T. B., born 15.10.59.

The second child of healthy parents. Pregnancy and delivery normal; birth weight 6 lb 15 oz. The first infant died with multiple congenital abnormalities.

The child was cyanosed at birth and remained so for three days. There was evidence of respiratory obstruction. He had marked in-suction and lay with his head extended. There was stridor. On direct laryngoscopy the larynx was seen to be normal. X-ray of the neck showed a generalized tracheal narrowing down to a minimum of 0·5 mm opposite the fourth cervical vertebra—the average anterior posterior diameter at this site is 5 mm. The narrowing of the trachea was most marked in the upper part as compared to the normal which is narrowest in the lower part.

The child was nursed in an incubator in high humidity and given prophylactic antibiotics. He gradually improved and the respiratory difficulty disappeared over the course of ten days. The stridor lasted for two weeks, but returned if the child had a cold and cough, and was accompanied by minimal in-suction. The follow-up X-rays showed that the trachea had grown to a diameter of 3 mm in four months. The child now weighs 22 lb and is very well.

Discussion.—The term "tracheomalacia" is used to describe this condition although it is inaccurate. The trachea does not in fact "waste". There are very few reports of the condition in the literature. Those post-mortem examinations that have been performed have shown various abnormalities of the cartilages of the trachea. The usual C-shaped cartilages are fused at varying intervals along the sides and bizarre mosaics formed. Sometimes a fenestrated tube is found. The rest of the bronchial tree is usually normal. The condition is not found with other respiratory tract cartilage abnormalities, such as lobar emphysema.

This child shows the prominent features of this condition, namely the respiratory difficulty with variable stridor, both inspiratory and expiratory, associated with a normal cry. The position of the child with the head fully extended is also characteristic. Attempts at flexing the head caused further diminution of the tracheal diameter, and consequent interference with respiration.

The diagnosis is made by a lateral X-ray of the neck to show the air passages. The postero-anterior X-ray usually fails to show any evidence of trachea at all, and a tomogram at this age is difficult. A tracheostomy is to be avoided as the lumen is so fine that intubation is almost impossible and any reactionary œdema might well occlude the trachea.

The most difficult period for the child is the early weeks. In the majority of reported cases the trachea grows fairly rapidly over the course of several months. This suggests that the pathology in the group which recover may be different from that described in the autopsy specimens. The principles of treatment in the early days are to prevent pulmonary infection and drying of the respiratory epithelium which may lead to formation of inspissated mucus. The use of an incubator is an essential part of the treatment; the humidity of the air should be high and strict barrier nursing should be instituted. Antibiotics should be given at the first suggestion of respiratory tract infection.

The following cases were also shown:

Family with Pseudohypertrophic Muscular Dystrophy.—Professor A. G. WATKINS.

Mitral Incompetence. Patent Ductus and Hypoplasia of Left Pulmonary Artery. Treated successfully by left thoracotomy with exploration of the mitral valve, left pulmonary artery and left lung, and ligation of the patent ductus arteriosus.—Mr. H. R. S. HARLEY.

(1) **Hydatid Disease of the Lung.** (2) **Subarachnoid Hæmorrhage due to Arteriovenous Malformation in left Occipital Lobe.**—Dr. RITCHIE JENKINS.

Polyarteritis Nodosa.—Dr. WILLIAM DAVIES.

(1) **Chronic Gaucher's Disease with Pancytopenia — Splenectomy.** (2) **Aplastic Anæmia.** (3) **Neuroblastoma — Massive Hepatomegaly —Remission following Biopsy and Vitamin B_{12}.**—Dr. P. T. BRAY.

(1) **Diabetic Neuropathy.** (2) **Histiocytosis-X.**—Dr. N. ROYSTON.

(1) **Steatorrhœa with Osteomalacia.** (2) **Cushing's Syndrome.**—Dr. P. FOURMAN.

Urinary Incontinence Treated by Colonic and Ileal Conduits (Two Cases).—Mr. R. A. MOGG.

Fibromyxosarcoma.—Dr. T. A. BRAND.

Hirschsprung's Disease of Large and Small Intestine.—Dr. O. P. GRAY and Mr. D. B. E. FOSTER.

(1) **Mast Cell Disease.** (2) **A Syndrome of Abnormally Broad Feet (Pes Latus) Associated with Nævi of the Flank.**—Dr. R. ISAAC.

(1) **Recurrent Obstructive Jaundice. Choledochal Cyst.** (2) **Recurrent Obstructive Jaundice. Stenosis (Possibly Congenital) of Common Bile Duct.**—Dr. F. NASH.

(1) **Fanconi Type Anæmia.** (2) **Two Cases of Adrenal Hyperplasia in One Family.**—Dr. J. JACOBS.

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Lancet (1958) **1**, 525

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Meeting 8
July 15, 1960

COMBINED SUMMER MEETING HELD AT THE UNIVERSITY DEPARTMENT OF PHYSIOLOGY, OXFORD

OTOLOGICAL SESSION

Recent Advances in the Electro-nystagmographic Investigation of Neurological Disorders of Ocular Movement

By C. S. HALLPIKE, F.R.C.P., F.R.S., J. D. HOOD, D.Sc., and E. TRINDER[1]

THE use of the corneo-retinal potentials for the recording of nystagmic eye movements is well established, and presents no great technical difficulties. Thus, the amplification used may be of the A.C. or resistance-capacity coupled type, which is easy to design and operate.

When, however, we come to the nystagmographic analysis of certain derangements of nystagmus and other ocular movements which are present in many of the organic affections of the VIII nerve system which we encounter in the course of our otoneurological work at Queen Square, certain new and difficult problems arise. In particular, we have to face the need for accurate recordings, not only of nystagmic and other transient eye movements but also of sustained deviations of gaze. For this the use of direct coupled amplification has been widely considered and attempted. But the technical difficulties, arising in particular from voltage fluctuations within the amplifier and at the electrodes themselves, have proved insuperable and, so far as we know, no amplification system of this kind has yet been found of practical value for electro-nystagmography. The use of what is known as the "chopper" system of direct current amplification, combined with improvements in electrode design, now makes it possible to overcome these difficulties and to construct an electro-nystagmographic system of very high gain, combined with remarkable stability and freedom from distortion. For full technical details of the design, construction and performance of this equipment, reference should be made to another publication (Hallpike, Hood and Trinder, 1960, *Confin. neurol., Basel*, **20**, 232).

With such a system we have found it easy to record eye deviations of 1 degree of angle. In addition, sustained deviations of gaze can be accurately recorded with the eyes open, closed, or in darkness.

In Fig. 1 are shown some recordings which illustrate the performance of our equipment and the extent to which this can be made to surpass that of the conventional type of electro-nystagmograph based upon A.C. amplification.

The recordings are of the nystagmic response of a normal subject to a standard caloric stimulus $-30°$ C applied to the right ear for 40 seconds. A.C. amplification was used for the upper group of records, amplification of the chopper type for the lower group.

In both groups the subject's eyes, open, were directed in succession to the right, straight ahead, and to the left. The nystagmus is to the

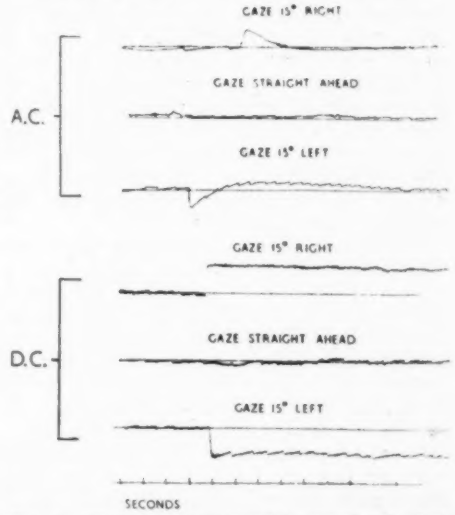

FIG. 1.—Electro-nystagmographic records of caloric nystagmus (*see* text).

[1]From the Otological Research Unit, Medical Research Council, National Hospital, Queen Square, London, W.C.1.

left and it will be seen that it is present only with the gaze directed to the left or straight ahead. It is, in fact, 2nd degree vestibular nystagmus to the left.

Now, in the case of the A.C. recordings, the gaze deviations to the right and left are denoted by no more than transient shifts of the base line. With the chopper recordings, however, it will be seen that as the gaze direction is altered and maintained, there occurs an easily read and maintained deviation of the tracing from the base line.

The point conveyed by these records has considerable practical significance—namely, that with this variety of amplification, in addition to the recording of nystagmus, we can achieve something impossible with A.C. amplification—relate the nystagmus to sustained deviations of gaze. This is important.

As we know, nystagmus resulting from peripheral vestibular disturbances is strikingly affected by the direction of gaze. It is exaggerated, as can be seen in the lower tracings of each group of records shown in Fig. 1, by gaze in the direction of the rapid component of the nystagmus, and inhibited by gaze in the opposite direction. It is indeed upon these factors that we base our conventional gradation of the magnitude of vestibular nystagmus, 1st degree, 2nd degree and 3rd degree.

FIG. 2.—Equipment and test procedure for electro-nystagmographic investigation of spontaneous nystagmus (*see* text).

One of the vital steps of a clinical otoneurological examination is the examination of the eyes for spontaneous nystagmus and, if this is found to be present, the assessment of its quality and magnitude. This is usually carried out by direct scrutiny of the subject's eyes in the upright position of the head. With our chopper system of amplification, however, it is possible to carry out the whole examination nystagmographically, and we have accordingly developed our test procedure upon these lines.

This has one obvious and immediate advantage, namely the provision of accurate and permanent records of spontaneous nystagmus. But this is not, we consider, the most important advantage. The nystagmic behaviour of the open eyes often tells less than the whole story, and indeed, as Aschan and Bergstedt (1955, *Acta Soc. Med., Upsal.*, **60**, 1) have so clearly shown, a certain pattern of spontaneous nystagmus, observable with the eyes open, may exhibit great changes when the eyes are closed or in darkness. The neurological factors which determine these changes are, as yet, ill-understood. Nevertheless, their clinical importance cannot be doubted, and for their detailed analysis it is clear that electronystagmography is indispensable.

Now, whether our examination of spontaneous nystagmus is carried out with the eyes open, closed, or in darkness, the influence upon nystagmus of gaze deviation remains a point of great importance, and in this respect the special characteristics of our present recording system have proved of vital importance.

Figs. 2 and 3 illustrate our technique for the electro-nystagmographic investigation of spontaneous nystagmus.

In Fig. 2 the patient, wearing the electrode assembly on a light plastic spectacle frame, is shown seated in a chair, the seat of which can be raised or lowered by means of a hydraulic jack. In this way the chin level is adjusted to a fixed and rigidly mounted chin rest.

With the chin in position, a hinged support is brought forward on to the occiput, and the head is thus comfortably and effectively immobilized. The vertical bar, shown to the front of the patient, carries a mark upon which he fixes his gaze. The bar with the fixation mark can be deviated to the patient's left or right by means of a handle which is controlled by the examiner, seated behind the

FIG. 3.—Same as Fig. 2.

patient, where he is able at the same time to observe the nystagmograph pens and operate the nystagmograph controls.

In Fig. 3 is shown another view of the equipment. For convenience, the deviations of the fixation mark are arranged in fixed steps of 10 degrees—10, 20 and 30 degrees—to the patient's left and right, and by means of his touch sense alone the examiner is enabled to set the deviation of the fixation mark, and accordingly of the eyes, to any of the points within this range.

This is effected by means of a spring-loaded ball which is carried upon the handle and engages a series of recesses suitably spaced along the circumference of a steel half-circle.

This provision is, of course, essential when the need arises for the patient to deviate his gaze in darkness. The procedure then is as follows: The patient rests his hand upon a support carried on the bar below the fixation mark with his thumb tip extended to cover the mark, as shown in Fig. 3. So arranged, the patient is then required to fix his gaze, in total darkness or with eyes closed, upon his thumb tip, which can then be deviated by the examiner to the various set points to left or right. During this examination local lighting, carefully screened, is provided for the recording pens which can thus be kept under observation by the examiner. Under these conditions, it is found that a normal subject, using his joint-muscle sense, can follow the fixation mark with his eyes with very considerable accuracy.

In Fig. 4 is shown a schematic diagram of the recording pens, with their axes coincident and their writing points practically so. The outer pen records the angular deviation of the fixation mark from its straight ahead position. Upward and downward movements of the pen from the central base line correspond respectively to deviations of the fixation mark to the right and left.

The inner or eye pen, records the conjugate eye movements in the horizontal plane. The sensitivity of the amplification is adjusted to correspond with that of the other, or fixation mark pen. Both pens work to the same central base line.

It will be seen that as the fixation mark pen deviates from right to left, the eye pen follows it closely. The recording being made is from a subject with 3rd degree vestibular nystagmus to the left. Thus, with fixation on the mark at 20 degrees to the right, the eye pen shows slight nystagmus, which is much increased when the eyes follow the deviation mark to 20 degrees left.

This arrangement of the pens has two advantages. Firstly, each pen is able to operate across the full width of the paper which can be correspondingly narrow. Secondly, the coincidence of the pens makes it easy to observe at any point on the record, the accuracy with which the eyes are maintaining their prescribed deviation.

The results obtained with this equipment are illustrated by the records shown in Figs. 5–7.

Three subjects were used. The first (Fig. 5) was normal. The second (Fig. 6) exhibited spontaneous nystagmus following unilateral labyrinth destruction for Ménière's disease. In the third (Fig. 7) spontaneous nystagmus was also present, resulting from a tumour of the right cerebello-pontine angle, with early involvement of the vestibular elements within the brain-stem.

In the top record of Fig. 5 the subject, with his eyes open, first fixes his gaze upon his thumb in the straight ahead position. When the thumb is deviated 20 degrees to the right it will be seen that his eyes follow it accurately. Between the points, "eyes closed" and "eyes open", the subject's eyes are closed and it will be seen that, apart from a few small irregularities, the gaze deviation is accurately maintained.

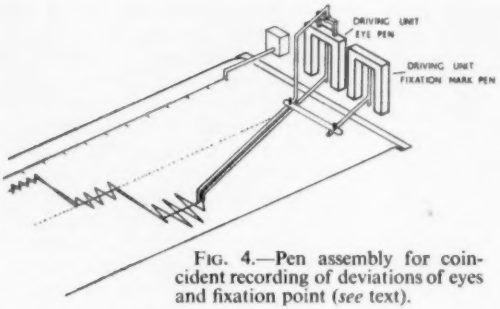

FIG. 4.—Pen assembly for coincident recording of deviations of eyes and fixation point (*see* text).

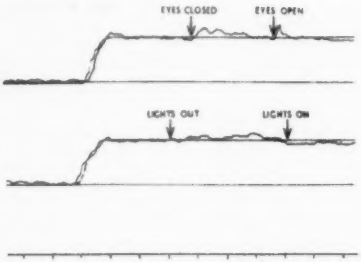

FIG. 5.—Normal. Gaze deviation 20 degrees right fixation on thumb.

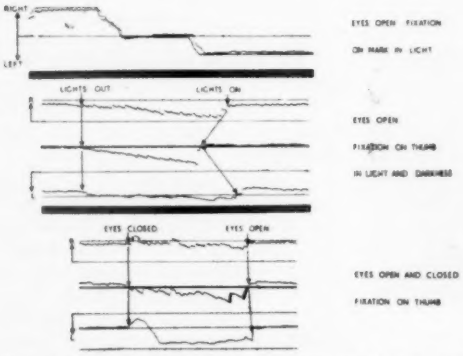

FIG. 6.—Left Ménière's disease. Destruction of left labyrinth. 2nd degree nystagmus to right.

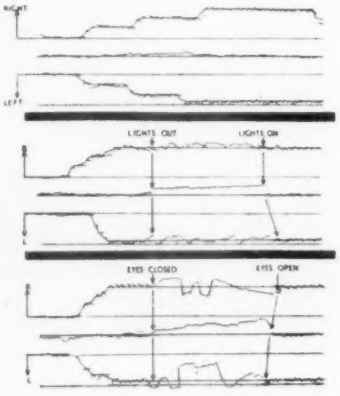

FIG. 7.—Right acoustic neuroma. 2nd degree nystagmus to left. 1st degree nystagmus to right.

The lower record shows the same sequence with one difference, visual fixation being eliminated, not by closure of the eyes, but by darkness. It will be seen that under these conditions, too, the gaze deviation is accurately maintained.

In Fig. 6 are shown the results of a nystagmographic study of the spontaneous nystagmus resulting from unilateral labyrinth destruction for Ménière's disease.

In the top record (centre) the eyes are open in the light with the gaze straight ahead. Slight spontaneous nystagmus to the right is just discernible upon the base line. This is more marked with the gaze to the right and absent with gaze to the left. In conventional terminology there is 2nd degree nystagmus to the right. It will be noted how steadily the gaze follows the fixation mark throughout.

In the middle and bottom sets of records the effects upon the spontaneous nystagmus of the elimination of visual fixation can be studied. This is achieved either by darkness or by eye closure; under both conditions the deviation of the eyes is controlled by fixation upon the thumb tip.

The middle set of records will first be considered. Darkness was used for the elimination of visual fixation. The middle tracing starts with the gaze straight ahead. At the "lights out" point, indicated by the arrow, there is a slow drift to the left, i.e. in the direction of the slow component of the spontaneous nystagmus. The nystagmus is markedly facilitated.

The same drift to the left, with facilitation of spontaneous nystagmus in darkness, is exhibited in the top tracing which starts with the eyes deviated 20 degrees to the right.

In both tracings, too, these effects are abolished by the restoration of visual fixation.

The bottom tracing starts with the eyes deviated to the left; in darkness, slight additional deviation occurs with definite nystagmus to the right. In other words, 3rd degree nystagmus to the right is present in darkness.

In the bottom set of records, eye closure was used for the elimination of visual fixation, and the results, as will be seen, are not quite the same. The middle tracing starts with gaze straight ahead, the top tracing with the gaze deviated

20 degrees to the right. Both of these tracings certainly show some increase of nystagmus with the eyes closed. The nystagmus seen, however, is far less regular in character than that observed in darkness.

The bottom tracing begins with the gaze deviated 10 degrees to the left, and it will be seen that when the eyes are closed they take up a position of extreme deviation to the left without nystagmus.

The conclusion to be drawn from these records is that in spontaneous nystagmus of this kind due to a labyrinthine lesion, the elimination of visual fixation by darkness certainly facilitates the spontaneous nystagmus, a point already emphasized by Aschan and others. In addition, there occurs a marked deviation of the eyes in the direction of the slow component of the nystagmus.

If, however, we use eye closure instead of darkness to eliminate visual fixation, the results are not quite the same. Though the cause of this difference is not at present clear, the fact that it exists would certainly seem to be a matter of some practical importance, and emphasizes the need in studies of this kind for exercising discrimination in the choice of eye closure or darkness for the elimination of visual fixation.

In Fig. 7 are shown the results of a similar nystagmographic study of the spontaneous nystagmus in a subject with a right acoustic neuroma with early involvement of the vestibular elements within the brain-stem. In the straight ahead position of gaze, slight spontaneous nystagmus is present to the left.

With visual fixation, the gaze is now deviated to the left, and the nystagmus increases in amplitude and frequency. With deviation to the right, there is a well-marked nystagmus to the right. There is, in fact, 2nd degree nystagmus to the left and 1st degree to the right, a familiar finding with an acoustic neuroma at this stage of its development.

In the middle and lower sets of records the effects of eliminating visual fixation have again been studied. For the middle set of records darkness has been used.

The middle tracing starts with the gaze straight ahead. At the "lights out" point the eyes drift slowly to the right in the direction of the slow component of the 2nd degree nystagmus. By contrast with the last case, however, there is no facilitation of spontaneous nystagmus, and in fact the nystagmus disappears.

Fixing on the thumb tip, the gaze is now deviated to the right and left. This deviation in darkness is, as will be seen, very well maintained. Both with deviation to the right and to the left, however, there is *no* facilitation of the nystagmus which, instead, becomes rather irregular.

In the bottom set of records are shown the results of eliminating fixation by means of eye closure. First of all, with the gaze straight ahead: As the eyes are closed, the gaze deviates slowly in the direction of the slow component of the nystagmus which is eliminated, promptly reappearing at the "eyes open" point with restoration of the straight ahead direction of gaze, when visual fixation is restored. With the gaze deviated 30 degrees to the right and left the effects of eye closure are as shown. In both cases the spontaneous nystagmus to the right and to the left is seen again at the right of the record, when visual fixation is restored.

Discussion

The nystagmographic features of the spontaneous nystagmus revealed in the last two of our three subjects, arising in one case from a peripheral and in the other from a central vestibular disorder, are clearly both complex and obscure. Nevertheless, as the records show, certain points of difference are evident, and would appear to be of considerable neurological interest.

Thus, as we know, spontaneous vestibular nystagmus, as seen on direct inspection of a subject's eyes, may be caused by organic lesions at a variety of points within the vestibular system, including the labyrinths, the vestibular nuclei, the cerebellum, and even the cerebrum, as in certain cases following hemispherectomy.

The possibility of effecting a differentiation of these lesions upon the basis of differences in the characteristics of the nystagmus itself is clearly a matter of considerable practical importance. Suggestions that such differences exist have long been available. Thus, although the abolition of fixation by means of Frenzel's glasses is known to increase the nystagmus of a peripheral lesion, Holmes (1917, *Brain*, **40**, 461) pointed out that it decreased nystagmus due to a cerebellar lesion.

Here a technical difficulty of some importance arises. Abolition of fixation, whether by means of Frenzel's glasses or otherwise, may be and often is accompanied by changes in the deviation of the eyes, and it may well be to this rather than to the abolition of retinal fixation that the effect upon nystagmus is due.

Now, using electro-nystagmography as we have done, we can abolish retinal fixation by means either of eye closure or darkness, and at the same time control and record eye deviations.

In this way, it should be possible to effect a fuller analysis of the effect upon nystagmus of these two variables, and so extend the diagnostic value of electro-nystagmography.

The Effects Upon Vestibular Function in the Cat of Unilateral Destruction of the Nucleus Fastigii

By C. S. Hallpike, F.R.C.P., F.R.S., and C. R. Pfaltz, M.D.[1]

Introduction

In 1952 Dix and Hallpike published a detailed account of the otoneurological findings in 100 subjects who exhibited positional nystagmus of a type first described in 1921 by Bárány. In view of the paroxysmal character of the nystagmus and the benign course of the disorder, Dix and Hallpike termed this condition the "benign paroxysmal type" of positional nystagmus.

Like Bárány, they found no evidence of an organic affection of the nervous system central to the labyrinth, and agreed with Bárány in attributing the positional nystagmus to a lesion of the otolith apparatus. This view they were able to support by the finding in a typical case of certain histopathological changes in the otolith apparatus of the ear placed undermost in the critical test position. Similar clinicopathological findings in another subject who exhibited the same type of positional nystagmus during life were reported in 1957 by Cawthorne and Hallpike.

Thanks to the work of Nylén (1931) we know that positional nystagmus may also result from organic affections of the central nervous system within the posterior fossa.

Patients so affected usually differ in a number of ways from those exhibiting the benign paroxysmal type of positional nystagmus. Firstly, obvious clinical evidence is usually present of widespread and serious organic disease of the central nervous system; most commonly malignant disease, primary or secondary, or disseminated sclerosis. It is seldom, therefore, that it can be said of these patients that their lesions are limited and will not shorten life.

The character of the nystagmus, too, is important. As a rule it develops promptly in the test position, is well sustained and unaccompanied by any or much vertigo. Its direction is frequently altered if the head position is changed, and in this it exhibits Nylén's direction-changing characteristic.

Great difficulties beset our approach to the problem of its precise morbid anatomy and neural mechanism. Firstly, post-mortem material is difficult to obtain. The disease process, too, tends to be widespread, progressive and long continued. Post-mortem examination may, therefore, be deferred for months or years after the last functional tests, and the correlation of their results with the structural changes is thus rendered very difficult indeed.

For this reason it has been necessary to resort to animal experimental studies, and a good deal of evidence obtained in this way is already at our disposal. Thus, in 1942, Spiegel and Scala were able to report the occurrence of positional nystagmus in cats as a result either of partial destruction of the lobus posterior medianus, or of electrolytic lesions of the nuclei tecti of the cerebellum.

Carréa and Mettler (1947) reported the results in primates of extensive removal of the cerebellar cortex and deep cerebellar nuclei. They concluded that lesions of the posterior part of the nuclei fastigii had much the same effect upon vestibular function as lesions of the vestibular portion of the cerebellar vermis. They noted, in particular, the occurrence of positional nystagmus following extensive destruction of the vermis and nuclei fastigii. Botterell and Fulton (1938), however, also working with primates, never observed positional nystagmus following unilateral or bilateral destruction of the nuclei fastigii.

In some of the experimental work to which we have referred, the technical methods would appear to have lacked precision, and to this it may be justifiable to attribute the inconclusive character of the results.

More recently, however, experiments designed to produce positional nystagmus in cats, and carried out with greater precision by means of stereotaxically induced lesions of the cerebellum, have been reported by Carpenter *et al.* (1958) and by Fernandez *et al.* (1959).

Present Work

In the course of the work now to be described we have ourselves studied the effect upon vestibular function in the cat, with particular reference to the occurrence of positional nystagmus, of unilateral destruction of the nucleus fastigii. This work was carried out early in 1953 during the tenure by one of us (C. R. P.) of a whole-time grant from the Medical Research Council.

Methods and Material

The nuclei fastigii, as represented by Clarke and Henderson (1914), consist of elongated columns of nerve cells, some 2·0–2·5 mm in diameter, and some 4–7 mm in length, with their long axes at right angles to the coronal plane, and their centres some 1·5–2·0 mm to each side of the mid-line. The sections of the cat's brain

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and brain-stem, which Clarke and Henderson used for their stereotaxic analysis, were also cut in the coronal plane. They thus provide a particularly clear display of the nuclei fastigii, which greatly simplifies the stereotaxic approach thereto. The vestibular affinities of the nuclei fastigii are, of course, well authenticated. Fig. 1 (taken from Jakob, 1928) shows the connexions between the nuclei and the vestibular nuclei by way of the cerebellum.

For our operations we used a stereotaxic apparatus which incorporated a number of new features. These, in addition to making possible an accurate and speedy stereotaxic approach to the various structures within the brain and brain-stem, greatly facilitated the preliminary surgical procedures. Means were also provided for ensuring that the final histological sections of the brain and brain-stem were cut in the coronal plane, and in this way the histological study of the lesions was much simplified. The operations were carried out upon 3 adult cats, under intratracheal trilene and oxygen anæsthesia.

Results

Cat I.—Electrolytic destruction of the right nucleus fastigii.

The animal recovered well from the operation, and was walking about and eating well forty-eight hours later. It was anæsthetized and subjected to intravital fixation on the fifth day. In the intervening period it was examined daily for spontaneous and positional nystagmus, and for abnormalities of posture and gait.

No abnormality of head posture was observed. There was, however, a tendency to deviate to the right in walking.

There was no spontaneous nystagmus with the head erect at any time, and no suggestion of positional nystagmus until the fifth day. Then, with the head back and to the right, we observed two nystagmic jerks to the right and, with the head to the left, two jerks to the left. This we regarded as insignificant.

Cat II.—Electrolytic destruction of the left nucleus fastigii.

When first seen on the morning after the operation, the animal exhibited definite positional nystagmus. With the head back and central, the nystagmus was directed vertically downwards. With the head back and to the right, there was some lateral nystagmus to the left. With the head back and to the left, there was some lateral nystagmus to the right. Under all conditions, the nystagmus was slow and disappeared slowly if the test position was maintained.

At the time of the examination the animal was still drowsy, and we accordingly thought it possible that the nystagmus was due to the Nembutal anæsthetic used in this animal. This was confirmed on re-examination two-and-a-half hours later. The positional nystagmus had then disappeared and was not seen again within the period preceding intravital fixation on the fifth day. Spontaneous nystagmus with the head erect was not seen at any time. Some loss of tonus of the left limbs was noticed on the first three days after the operation. It then disappeared, and thereafter the animal seemed quite normal.

Our conclusions were that in neither of these animals had positional nystagmus been caused by the operation.

Histological findings.—As usually happens, the middle ears in both animals were found to have been damaged by the fixation pins of the stereotaxic apparatus. The labyrinths, however, were normal.

In Fig. 2 is shown a low-power photomicrograph of the lesion in Cat No. I. The left nucleus fastigii is well shown. The right nucleus fastigii has been cleanly destroyed.

In Fig. 3 is shown a reconstruction, based upon a study of serial sections of the nucleus, which outlines the exact extent of its destruction.

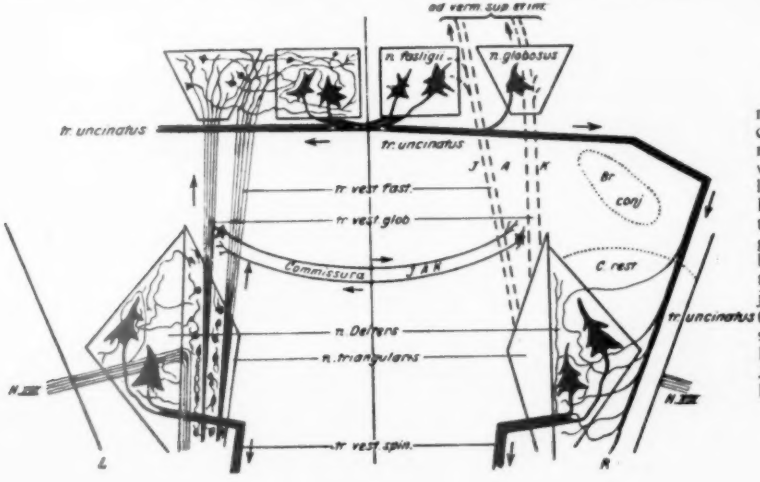

FIG. 1.—Schematic representation of the connexions of the nucleus triangularis with the contralateral nucleus of Deiters by way of the vestibulo-fastigial, vestibulo-globosal and uncinate tracts. JAK = corpus juxtarestiforme. (From Winkler, slightly modified. Reproduced from Jakob, 1928, by kind permission.)

In Fig. 4 is shown a low-power photomicrograph of the lesion in Cat No. II. The left nucleus fastigii has been cleanly destroyed.

In Fig. 5 is shown a reconstruction based upon a study of serial sections of the nucleus which outlines the exact extent of its destruction.

Cat III.—In this animal we endeavoured to destroy the right nucleus fastigii. On the day following the operation some vertical nystagmus downwards was observed in the supine position, with the head central or turned to the left. Two days later this nystagmus had disappeared and was not observed again within the period up to 15 days following the operation, when the animal was sacrificed. During this period the animal showed considerable loss of tonus of the right limbs, with a tendency to fall to the right. The brain-stem and cerebellum were prepared for examination by means of the Marchi procedure.

Histological examination revealed an extensive electrolytic lesion involving the lateral part of the anterior end of the right nucleus fastigii, with extension into the surrounding white matter. Numerous degenerated fibres were seen in the posterior vermis, in the left paramedian lobe, in the uvula and in the commissura inter-fastigialis. Degenerated fibres could also be traced in all three cerebellar peduncles on the right side. Fibre degeneration was also present within the uncinate tract on the left side and in the olivo-cerebellar tracts on both sides. The distribution and extent of the degenerative changes in the brain-stem and cerebellum are shown in Fig. 6.

FIG. 4 (*Cat II*).—Section of brain-stem and cerebellum. Marchi staining; showing electrolytic destruction of left nucleus fastigii.

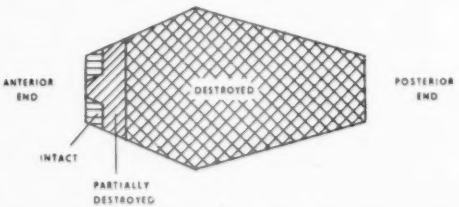

FIG. 5 (*Cat II*).—Left nucleus fastigii. Reconstruction. Horizontal section. Overall length of nucleus 4·4 mm.

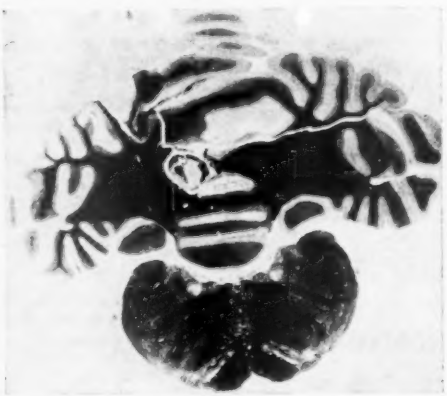

FIG. 2 (*Cat I*).—Section of brain-stem and cerebellum. Marchi staining; showing electrolytic destruction of right nucleus fastigii.

The operative technique used for this animal was not so satisfactory as that used for the other two. In addition, the area of destruction found in animal No. III was a good deal more extensive and involved not only the nucleus fastigii but also a considerable part of the surrounding cerebellar tissue.

We are, therefore, inclined to conclude that the slight positional nystagmus noted in this animal was due not to the destruction of the nucleus fastigii but to the widespread damage around it.

Discussion

Although our material was very small, and our results negative, they were nevertheless very

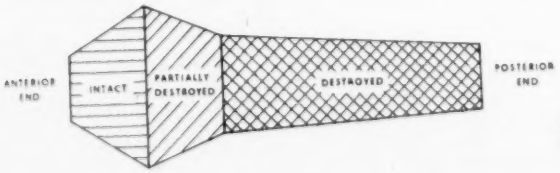

FIG. 3 (*Cat I*).—Right nucleus fastigii. Reconstruction. Horizontal section. Overall length of nucleus 6·5 mm.

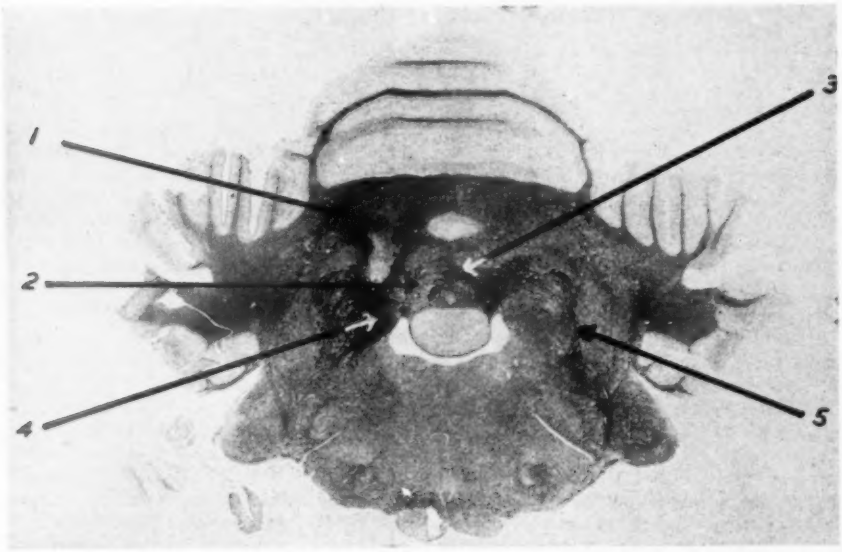

FIG. 6.—Low power photomicrograph (×5). Marchi stain. 1. Area of electrolytic destruction in the right paramedian region. 2. Posterior extremity of right nucleus fastigii. 3. Degenerate fibres within the interfastigial decussation. (Tractus nucleo-cerebellares). 4. Ipsilateral degeneration of nerve fibres descending into the right restiform and juxtarestiform bodies. 5. Contralateral degeneration of nerve fibres descending into the left restiform and juxtarestiform bodies.

clear-cut and because of this they seem to make possible a conclusion of some value: that positional nystagmus of the central type cannot be related to lesions of the nuclei fastigii. In respect of technique and pathological findings our results accord well with those of Carpenter *et al.* (1958), who also carried out stereotaxic destruction of the nucleus fastigii in the cat on one or both sides. Their description of the degenerative changes in the cerebellum and brain-stem, as traced by means of the Marchi method, differed little from that which we have observed. They noted, too, the occurrence of ataxia with deviation to the side of the lesion when this was unilateral. Spontaneous nystagmus seems to have been a negligible feature of the after-results of the operation, and no reference is made to the occurrence of positional nystagmus.

We come, finally, to the work of Lindsay and his co-workers in Chicago (Fernandez *et al.*, 1959) who have been successful in inducing positional nystagmus in the cat by means of surgical ablation of the nodule. They attribute the occurrence of positional nystagmus to the abolition of inhibitory influences normally exerted by the nodule upon the vestibular nuclei.

From the point of view of practical oto-neurology, it is clear that the evidence sought from these animal experiments is something that will make it possible to localize the site of lesions in the brain-stem or cerebellum which are responsible in patients for the very important physical sign of positional nystagmus of the so-called central type. All that can be said upon this point is that our own slight contribution clearly points away from the nucleus fastigii. The more extensive investigations of Lindsay and his colleagues point towards the nodule.

Acknowledgments—The authors wish to express their indebtedness to the late Mr. F. J. F. Barrington, F.R.C.S., for advice and assistance most generously provided in the early stages of this work.

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The Innervation of the Middle Ear

By Professor MICHELE ARSLAN[1]

This paper presents the result of research work carried out in my Department, under my direction, by Dr. Vittorio Bötner, Dr. G. Pivotti and others. Dr. Bötner has accomplished the greater part of the work, with the co-operation of the Institute of Anatomy, and his book (1959) records also many references to the reported results of other workers in this field. Our aim was: (1) To produce evidence of the real nature of some nerves existing in the middle ear. (2) To clarify the function of the twigs of the tympanic nerve, connecting it with the carotid plexus and the system of the petrosal nerves. (3) To establish the relationship between the somatic and the autonomic nerves of the middle ear.

We must be aware of the inadequacy of our knowledge of the morphology of the middle ear nervous structures. There are many obscurities as to the origin of the nerves, the destination of their fibres and their connexions with other nerves passing through or near the middle ear. Above all, as much as histologic investigation is able to tell us, it seems necessary to establish either the somatic or the sympathetic nature of every trunk really belonging to the middle ear: at present, there is great confusion of opinion on this point.

We may also enquire as to the reasons that have hampered the development of more analytic morphological investigations on the nerves of the middle ear, in comparison with the progress attained in the anatomical knowledge of other parts of the peripheral nervous system.

The answer is that too many difficulties face the anatomist who wants to carry out researches in the middle ear region: (*a*) Technical difficulties concerning the histological preparation (decalcification, &c.) of the temporal bone; (*b*) variability of the anatomical features: (*c*) lack of physiological knowledge of the specific function of every nerve belonging to the middle ear.

The premises and considerations hitherto exposed, which explain briefly the need for a more thorough morphological study of the nervous region here examined, first of all suggest the necessity of adopting methods and techniques which are able to supply pictures allowing at the same time an analytic and yet all-embracing survey of the different trunks and a comprehensive view of the entire nerve supply of the middle ear.

In order to fulfil this need, we carried out researches first on the embryo, in which it is possible to analyse, with specific methods, the origin of the nervous fibres, the course of nerve connexions between different fibre groups, which run either independent or joined with synapsis, fibre changes between nerves and twigs. These details are easier and simpler to notice in the embryo, which offers a more compendious panorama; and therefore, they can be analysed more clearly and often are better able to be interpreted in comparison with the histological research performed on temporal bones of young and adult men.

Secondly it was necessary to verify, in various species of mammals, the anatomical differences in the middle ear nerves, establishing the possible topographic, structural and functional variations in relation to the phylogenesis.

To this end, researches were conducted both on embryos and mammals, belonging to different species, and in different periods of embryonal development, dealt with by specific methods.

Among the results obtained with our numerous researches, I shall try here to explain only some of them which seem to us of particular interest.

On the Tympanic Nerves

In man, the number and the disposition of the branches of the tympanic nerve, which make up the tympanic plexus visible to the naked eye, or with a little magnification, are very variable.

Rosen, in a systematic investigation performed on 100 cadavers, analysed the variability of the constitution of the tympanic plexus. According to this author, the tympanic nerve usually runs along the surface of the promontory; only in 19 cases was it contained in a little bony canal. In 86 cases an anastomotic branch between the tympanic and the facial nerve was noticed. There was observed in 58 cases a collateral branch to the oval window; in 65, a branch directed to the round window; in 38 a branch directed between the two windows; in 97 cases, a collateral branch directed to the tube and an anastomosis with the carotid plexus.

We can summarize the results of our investigations in the following way. The branches that the tympanic nerve yields along its course through the cavity of the middle ear may be divided into *anastomotic* and *terminal*.

From the evaulation of the average data concerning the number, the topography and the end of the branches of the tympanic nerve, taking into account the variability they may display (Rosen, Frenkner, Portman and Puig), we may assume that the human tympanic nerve constantly sends its branches: (1) To the eustachian tube, directed in a rostral sense; (2) to the oval window; (3) to the mastoid cells; (4) to the round window or near it; (5) to the facial nerve (Fig. 1).

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FIG. 1.—Tympanic nerve (n.t.) and its branches: to the tube (r.tu.) and between the two windows (r.p.). · 45. Human embryo 43 mm C.R. c.t.t., eustachian tube; m.t., tympanic membrane; P., peri-otic bone; M., malleus; o.i., inner ear, S., stapes; m.s., stapedius muscle; VII, facial nerve. (These abbreviations apply also to Figs. 2, 3, 6 and 10.)

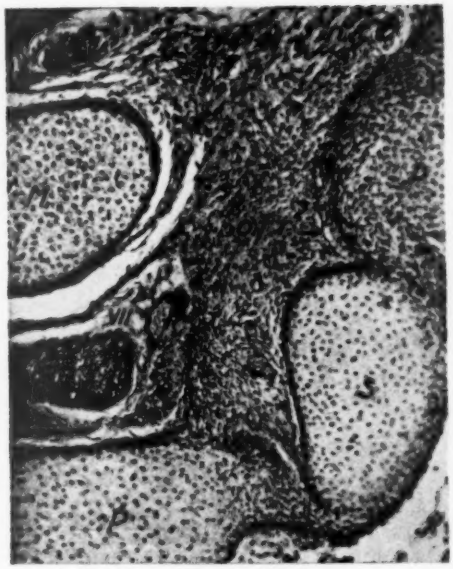

FIG. 2.—Branch arising from the tympanic nerve (n.t.), directed to the oval window (o.f.r.). × 150. Human embryo 43 mm C.R. o.f.r., branch of the tympanic nerve directed to the oval window.

The terminal branch of the tympanic nerve beyond the tympanic cavity reaches the otic ganglion as the lesser superficial petrosal nerve.

Our observations largely confirm what is already known concerning the origin, the course and the termination of the tympanic nerve. But I want to point out some details of the distribution and nature of the branches of this nerve, as revealed by Bötner's investigations.

Among the posterior branches of the tympanic nerve, the one which could be best observed in all the temporal bones examined, is that directed to the oval window, within which it was seen to be distributed. The branch directed to the round window appeared less constant: in some specimens only some isolated nerve fibres could be recognized. In four temporal bones, a branch in a dorsal direction toward the portion of the promontory which lies between the two windows was observed (Fig. 2).

Among the rostral branches, a branch directed to the tube also appeared constant.

The caroticotympanic anastomosis, at times single, at times double, deserves a detailed analysis. The literature concerning the caroticotympanic connexions does not supply uniform interpretations on the nature of the fibres of which it consists. According to some authors, the caroticotympanic nerves may be formed by fibres coming from Jacobsen's nerve; according to others, by fibres from the sympathetic pericarotidian plexus to Jacobsen's nerve.

In fact, the first hypothesis assumes that the branch coming from the IX nerve descends along the internal carotid artery till it reaches the origin of the vessel, contributing in this way to the formation of the perivascular plexus.

In our investigations in one specimen, the caroticotympanic anastomosis was seen to originate directly from Andersch's ganglion, near the origin of the tympanic nerve. However, in all cases the anastomosis is formed by fibres which have almost all the histologic and morphologic features of the tympanic fibres, that is, of great size and intensely black-coloured: these fibres do not belong to the pericarotid ones because they are not sympathetic.

As for other branches of the tympanic nerve, in the embryos of 65 and 220 mm we have sometimes observed a branch directed to the greater superficial petrosal nerve; this fact was described by Vitali and other anatomists about fifty years ago. Although in this twig, a distinction based on the histomorphological features is not possible, nevertheless we got the impression that these fibres are given by the former nerve to the latter.

Therefore the anastomotic twigs and branches of the tympanic nerve have anatomical features

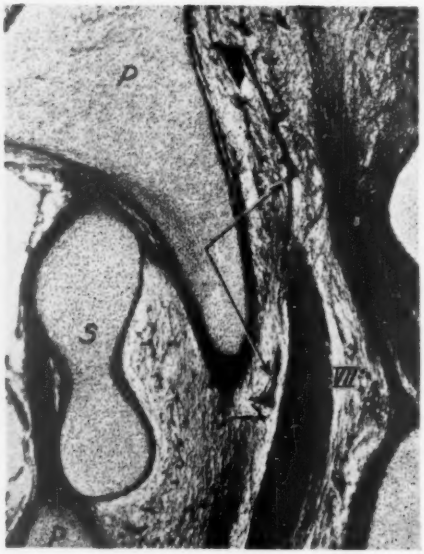

FIG. 3.—Autonomic branch (arrows), which runs parallel to the facial nerve (VII), and afterwards rejoins the tympanic ganglion. A small branch directed to the stapes (S) is also visible. × 40. Human embryo 65 mm C.R.

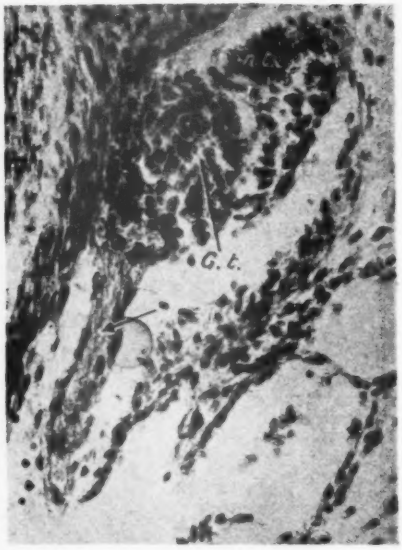

FIG. 4.—Autonomic branch (arrow), directed to the tympanic ganglion (g.t.). × 300. Human embryo 43 mm C.R. n.t., tympanic ganglion.

which may present different modalities, as was demonstrated by the researches carried out by Vitali and confirmed by our personal observations. Substantially, the anastomotic branches connect, in all cases, the tympanic nerve with the following nervous formations: (1) The sympathetic pericarotidian plexus, (2) the otic ganglion, by means of the lesser superficial petrosal nerve, (3) the facial nerve or one of its branches, (4) the oval window; (5) the round window or the region between the two windows.

On the Nervous Ganglia of the Middle Ear

The presence of small ganglia near the tympanic nerve and its branches, in man, has been studied by many authors. Vitali had already pointed out their presence and described their topographical features: a small ganglion, often also macroscopically visible, is placed near the tympanic nerve, where it enters the temporal bone: a twig connects this small ganglion with the facial nerve, at the level of its knee.

Another ganglion, smaller than the former one, is placed along the tympanic nerve, where the branch directed to the tube originates.

Vitali thought that these ganglia were of cerebrospinal nature, as Kolmer thought for similar nervous formations observed in the dog.

Eggston and Wolff described a tympanic ganglion along the tympanic nerve of one child and two adults. Portmann, observing the serial sections of temporal bones of human embryos, mentions the frequent finding of nervous ganglia along the branches of the tympanic plexus. Alexander and Marburg always found groups of ganglional cells in the region where the lesser superficial petrosal nerve is reached by a twig which joins it with either the facial nerve or the geniculate ganglion.

In all the branches of the tympanic plexus there may exist some ganglional cells, isolated or assembled in groups. These authors, too, mention the presence of a larger ganglion along the lesser superficial petrosal nerve.

In the opinion of Vitali, Alexander and Marburg, Kolmer (1927), the described ganglia along the branches of the tympanic plexus would be made up by cells with a T prolongation, and therefore of cerebrospinal nature.

Moreover, our observations on man confirm those on the human embryo, as much as concerns the constant finding of a ganglional formation placed near the tympanic nerve, on the medial face of the tensor tympani muscle.

Through the microdissection carried out on adult man, we could determine that this main tympanic ganglion lies in the anterior tympanic cavity; in order to visualize it, it is necessary to raise the tensor tympani muscle and to remove the thin bony wall which forms the channel in which the muscle is contained; the ganglion then

FIG. 5.—The middle ear of the hedgehog. × 18. 1, promontory; 2, round window; 3, tympanic nerve; 7, stapes; 8, stapedial artery which runs through the stapes crura; 9, tympanic artery; 10, malleus muscle.

FIG. 6.—The stapedial artery (a.s.) passing through the stapedial crura (S, S). × 30. Human embryo 65 mm C.R. g.t., tympanic ganglion.

appears like a fusiform enlargement. Another inconstant, much smaller, ganglional formation, was observed where the tympanic branch directed to the tube rises up. From the whole of the histomorphological data acquired on this ganglion and evidenced in the iconography, we think we can include the neurons of this tympanic ganglion in the III type of Cajal's classification. Therefore, they would be elements of surely autonomic nature, probably sympathetic, because of the presence of dendritic prolongations which are remarkably long.

As to the other much smaller groups of cells,

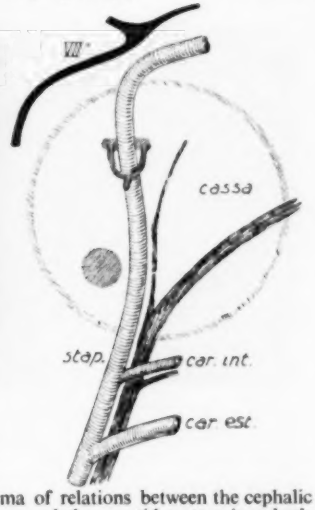

FIG. 7.—Schema of relations between the cephalic sympathetic nerve and the carotid system in a bat's embryo (25 mm C.R.). The stapedial artery, larger than the internal and external carotid, runs through the stapes, and will remain functioning after birth.

generally formed by few elements, which can be found occasionally along the tympanic nerve, in particular at the level of the origin of its branches, more frequently at the origin of the tubal branch, the analysis of the histomorphological features of the cells forming both the principal tympanic ganglion and the other minor ones, their comparison with ganglia belonging to other ganglia of known nature, would make us decide in favour of an autonomic nature of these tympanic ganglial formations. In all the embryos we have examined, the main tympanic ganglion receives, at its caudal pole, a bundle of autonomic fibres with a course parallel to that of the facial nerve for a certain part of its second and third portion. A twig of this branch ends at the stapes, accompanied by a small vessel which runs between the crura (Figs. 3 and 4).

Taking into account its course (that in some parts is the same as that of the stapedial artery), we might give an embryogenetic interpretation of this autonomic twig.

As is known, the stapedial artery disappears after embryonal life. There would remain its sympathetic equipment, which we can consider just as an autonomic nerve. In fact, it appears as a formation which, in the younger embryo, has the characteristic features of the vessels' perivascular fibres; while in the older embryo the same features are less noticeable (Figs. 5, 6 and 7).

On the other side, the fibres of the tympanic nerve do not visibly seem to stop in the tympanic ganglion. Moreover, within the tympanic ganglion originate some small fibres which, after

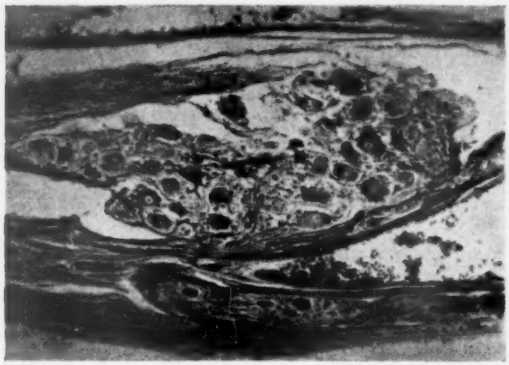

FIG. 8.—Tympanic ganglion in man (Cajal method). × 165.

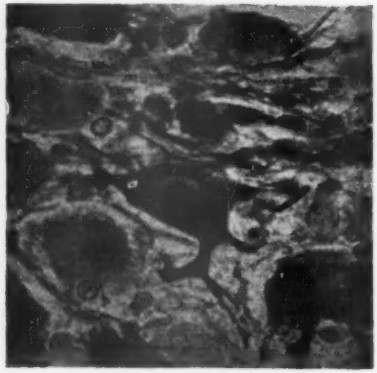

FIG. 9.—Detail from Fig. 8. × 900.

having reached the rostral pole of this formation, are mixed with these tympanic nerve fibres which at this point become the lesser superficial petrosal nerve; and so these nerves continue their course in a rostral sense together, directed towards the otic ganglion.

The considerations hitherto described, if on one side they establish the presence of important autonomic formations in the rostral part of the middle ear cavity, on the other hand support the concept that perhaps only a small part of these formations is directed to the middle ear in general, and to the oval window region in particular. The autonomic innervation of the latter would be rather originated by the described twig connecting the facial nerve with the tympanic ganglion.

The presence of this ganglial formation of the middle ear is little known; it was first described by Vitali. Therefore, it seemed advisable to investigate further its anatomical position and nature. The constancy with which this formation was found in man and animals indicates that its function is yet unknown: this ganglion probably takes part in the complex regulation of the movements connected with sound transmission of the structures of the middle ear (Figs. 8, 9 and 10).

On the Sympathetic Nervous Supply of the Middle Ear

The data now described give us a full confirmation of the sympathetic participation in the innervation of the middle ear, deriving from three sources: (*a*) The facial nerve; (*b*) the periarterial network; (*c*) some isolated trunks.

(*a*) An example of this origin is given by the stapedius nerve, whose autonomic fibres (after Foley) probably arise from the geniculate ganglion and which is included in the facial nerve.

(*b*) The perivascular source concerns all the arteries which are contained in the tympanic cavity, that is, according to Porta: (1) The stylo-

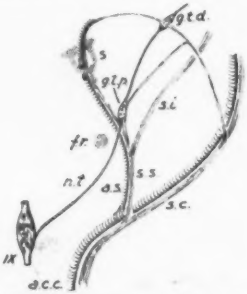

FIG. 10.—Tympanic plexus and its ganglia, in cat (schema). f.r., round window; s.c., carotid sympathetic; s.s., stapedial sympathetic; s.i., intratympanic sympathetic; g.t.p., proximate tympanic ganglion; g.t.d., distal tympanic ganglion; a.c.c., common carotid artery; a.s., stapedial artery; IX, glossopharyngeal nerve.

mastoid artery; (2) the tympanic artery; (3) the small branches of the middle meningeal artery; (4) the pharyngeal artery, which forms a very pronounced network on the promontory; (5) the caroticotympanic branch of the internal carotid artery. All these arteries carry orthosympathetic fibres, which are either distributed to the middle ear or cross this cavity (Figs. 11 and 12).

Recent investigations conducted by Schmidt, Moore and others, proved that the perivascular fibres are postganglionic, and soon leave the sympathetic ganglia to reach their final stations along the course of the arteries themselves.

Some investigators have pointed out the possibility that, in the caroticotympanic connecting branch, single fibres corresponding to postganglionic fibres derived from the superior ganglion reach the tympanic cavity to be distributed to the formations contained in it.

As for the sympathetic supply to the middle ear, Bötner's investigations in animals have revealed other interesting points on the problem, whose description is given in the author's book (Fig. 13).

FIG. 11.—Dog's temporal bone. The middle ear vessels have been injected with a special coloured solution (mercuric oxide). The oval and round windows are visible (on the right side) from the medial wall of the labyrinth: no vascular connexions between middle and inner ear are present.

FIG. 12.—As Fig. 11. The upper part shows the inner ear, the lower part the medial part of the middle ear: no vascular connexions are present between the two parts.

On the Innervation of the Middle Ear Muscles

We must admit for certain the existence of an autonomic efferent innervation of the ossicular muscles. As for the afferent component, described by several authors among the nerves supplying the ossicular muscles, we cannot deny that they are fibres which carry muscular proprioceptive impulses. They should stop in the geniculate ganglion and reach the brain-stem with the facial nerve.

The facial nerve, in fact, contains other afferent fibres which, as proved by physiological experiments, assure the conduction of impulses originated by muscular proprioceptors of the face.

It is well known that the reflex action of the ossicular muscles may be elicited by sound stimulations; the researches on this subject were carried out by Japanese (Esaki, Yasuo, Ochiai, Yasuie) and American (Weber, Vernon, &c.) authors.

Therefore, these reflexes, arising from the tensor tympani and the stapedial muscle, need afferent fibres, which may run in the tympanic nerve.

On the Innervation of the Tympanic Membrane

The drum's nerves are of sensory and autonomic type, and derive from different nerves. The external epidermal layer is supplied with branches originating from the auriculotemporal nerve, passing through the external acoustic meatus; this small branch, which runs down along the handle of the malleus accompanying a small artery, provides the sensory innervation of the superior two-thirds of the membrane. The sensory inner-

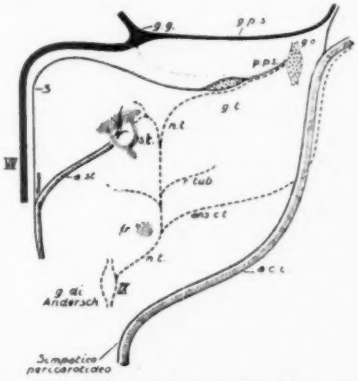

FIG. 13.—Schema of the branches of the tympanic nerve (n.t.), and of the carotid and stapedial sympathetic supply. S, autonomic fibres, which run with the facial nerve and, after leaving it, are directed to the tympanic ganglion. a.st., stapedial artery; g. di Andersch, ganglion of the IX nerve; ans.c.t., branch between tympanic nerve and carotid sympathetic; r.tub., tubal nerve; p.p.s., lesser superficial petrosal nerve; g.g., geniculate ganglion; g.p.s., great petrosal superficial nerve; g.o., otic ganglion; a.c.i., internal carotid artery; g.t., tympanic ganglion; st., stapes; VII, facial, IX, glossopharyngeal nerve.

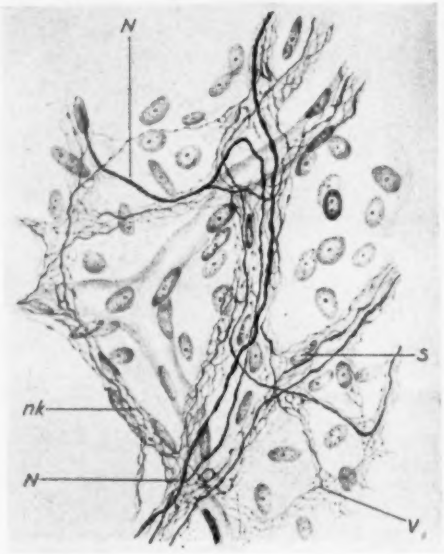

FIG. 14.—Man's drum. Bielschowsky method. × 400. Network of nerve fibres in connective tissue. N, somatic fibre; V, autonomic neurofibrillæ; S, Schwann nucleus; nk, nervous reticulum of a capillary wall. (After Andrzejewski.)

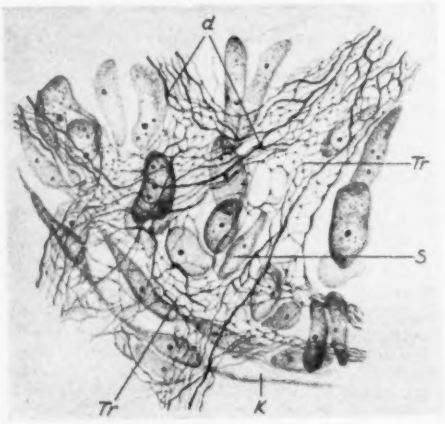

FIG. 15.—Man's drum. Bielschowsky method. × 1,100. Tr, terminal reticulum of the interstitial connective tissue; d, branching points of the neurofibrillæ; S, Schwann nucleus; K, capillary. (After Andrzejewski.)

vation of the inferior third is supplied by fibres of the nervus auricularis of the vagus. The mucous layer is reached by twigs of the tympanic plexus, that is, by fibres coming from the glossopharyngeal nerve and from the cervical sympathetic. Finally, we must remember the perivascular network, through which other autonomic fibres reach the tympanic membrane.

Andrzejewski in his research dedicated to the drum innervation, using the histological Bielschowsky-cross method, distinguishes myelinated fibres originating from somatic roots and other fibres supplied by the autonomic system. The myelinated fibres, at their origin course isolated, then in fibre division they lose the myelinated sheaths and from a more and more narrow plexus, placed in the fundamental substance of the fibrous layer of the tympanum; other small, much thinner, autonomic fibres also contribute to the formation of this plexus. Among the small tracts of autonomic fibres there exist direct anastomoses, which in this way give rise to a very narrow syncytial reticulum with characteristics of terminal nervous structure. In the mesh of this reticulum can be recognized the capillaries which have no innervation of their own, but which receive it from the terminal autonomic network which innervates the smooth muscle fibres, the connective tissue, and the glands (Stohr).

To the formation of the terminal nervous reticulum, described here, a great number of non-myelinated fibres contribute, coming from the dichotomy of myelinated fibres of cerebral origin (Figs. 14 and 15).

Conclusion.—The few results I have set forth certainly do not give a complete picture of all the nervous structures belonging to the middle ear, or which pass through it. We have investigated many other nervous formations, to clarify some very important problems: for instance, are there nervous branches connecting the middle ear with the inner ear? Do the parasympathetic and orthosympathetic fibres of the middle ear regulate the mobility of the ossicles and of the round window? Are there nervous mechanisms, as for example the tympanic glomus, that accomplish, in the middle ear, a hæmodynamic regulation, similar to that performed by the carotid glomus?

The middle ear is *the most important point of confluence and crossing of different nerves in the head*, a fact which proves the high functional and regulating importance of the auditory organ.

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(For other references to the literature *see* Bötner, 1959)

BOOK REVIEWS

Manual of Skin Diseases. By Gordon C. Sauer, M.D. (Pp. xvii + 269; illustrated, 28 colour plates. 70s.) London: Pitman Medical Publishing Co. Ltd. 1960.

There have been a number of recent dermatological publications designed for the general practitioner and student. This work is one of these and is well produced. It is a personal account of skin diseases written in a conversational manner and outlining treatment on first and subsequent visits. The reasons for the type of treatment chosen are explained so that even palliative treatment does not sound entirely empirical. The descriptions of diseases are good and easily understood.

There are many photographs including some in colour. Most are good but a few do not come up to the standard set by other recent publications.

A useful innovation in this work is the Dictionary-Index. In addition to giving the page number and illustration number of the items described in the main text it gives short notes on many other diseases and is a glossary of terms found in dermatological literature. It also acts as a classification for groups of diseases such as pigmentary disorders.

General practitioners and students will undoubtedly find this work of considerable value.

Basic Office Dermatology. By Stuart Maddin, M.D., Julius L. Danto, M.D., and William D. Stewart, M.D., F.R.C.P.(C.). (Pp. xix + 308; illustrated. 94s.) Springfield, Ill.: Charles C Thomas. Oxford: Blackwell Scientific Publications Ltd. 1960.

This book is designed for the general practitioner who wishes to treat his patients with dermatological diseases himself. It is arranged in six sections. The first section is by far the longest and describes the common skin diseases arranged in groups according to ætiology or presenting symptom. A uniform method of presentation is adopted and all descriptions are concise and readily understood. In this section standard treatments are given and in general proprietary preparations are recommended because of their standardization and the fact that they are readily obtained. This has obvious drawbacks where cost is important but is undoubtedly justified in many cases. Special investigations are mentioned where required and it is of interest to note that the author considers the demonstration of a mite in scabies "usually difficult". Illustrations consist of diagrams showing regional distribution of diseases and monochrome photographs most of which are satisfactory.

The second section consists of 16 colour photographs. Section three gives a brief résumé of diseases according to sites: face, hands, &c. Section four describes a few diagnostic procedures and section five describes in greater detail the principal methods of dermatological treatment. The final section describes cutaneous manifestations of internal diseases.

This book can be recommended to the general practitioner; medical students will also find it of great value although too long for routine use.

Leukæmia. Research and Clinical Practice. By F. G. J. Hayhoe, M.A., M.D.(Cantab.), M.R.C.P.(Lond.). (Pp. ix + 247; illustrated. 80s.) London: J. & A. Churchill Ltd. 1960.

The preparation of a monograph on leukæmia must be a formidable task. On the one hand so much is depressingly familiar to the audience—the clinical features, the hæmatological findings, the course and the responses to treatment—while on the other there is the enormous and confusing flood of experimental studies increasingly, possibly even mistakenly, centred around the animal rather than man. Dr. Hayhoe has obviously recognized this problem and principally by avoiding farouche speculation and unjustifiable extrapolation has succeeded in producing an objective, very well written and reasonably critical review of the diverse aspects of the subject. There is an excellent bibliography.

The Intestinal Tract. Structure, Function and Pathology in Terms of the Basic Sciences. By Richard Paul Spencer, A.B., M.A., M.D. (Pp. xvii + 411; illustrated. £5 2s.) Springfield, Ill.: Charles C Thomas. Oxford: Blackwell Scientific Publications Ltd. 1960.

The intestinal tract is a part of the body about which our knowledge remains very imperfect. In spite of much intensive study and new methods of investigation there are still big gaps in our understanding of intestinal function, especially of the small intestine. Dr. Spencer has set out to provide a reference book on this subject. He has aimed to collect and present the known data and to compile a comprehensive picture of available information.

Besides the factual details he has added comments and reviews both of others and his own which cover normal intestinal function and disease processes. This is not a textbook of gastroenterology, nor is it a critical review of one or more theories of digestive activity. It is a full and careful account of what is known at present about the intestinal tract with precise reference to

original sources of information, and is for this reason the more valuable. The chapter on absorption, for instance, which is one of the most important in the book, includes much new work and alone has nearly 200 references.

Other sections deal with Development and Innervation of the Intestine, Gastro-intestinal Enzymes, Disorders of Intestinal Function including accounts of Potassium Metabolism, Malabsorption, Wilson's Disease, Carcinoid and Studies of Protein Loss from the Intestine. This book covers a large field and gives the reader an easy chance to follow up problems in this field by providing him with basic information. It will be of most value to physicians especially interested in gastroenterology, but it will interest all practising clinicians and like all good reference books will put investigators in its debt.

Essentials of Fluid Balance. By D. A. K. Black, M.D., F.R.C.P. 2nd ed. (Pp. xii + 135. 20s.) Oxford: Blackwell Scientific Publications Ltd. 1960.

When Black's book was first published in 1957, it was regarded by many as one of the best introductions to water electrolyte balance written: the three years since then have not shown any reason for this opinion to be modified, and a second edition is very welcome: it is a testimonial to the up-to-dateness of the first edition that no major alteration has been required, and the changes are chiefly re-writing of some sections and a number of new references. The author mentions somewhat apologetically that he has not considered magnesium in this edition. By the time the next edition is called for the position of magnesium in the field of electrolyte balance will be clearer, and its repercussions will certainly have to be considered. However, for anyone who wants a scholarly introduction to a somewhat difficult subject, and is prepared to read carefully, Black's book still maintains its place.

Principles of Public Health Administration. By John J. Hanlon, M.S., M.D., M.P.H. 3rd ed. (Pp. 714; illustrated. 78s. 6d.) St. Louis: The C. V. Mosby Company. London: Henry Kimpton. 1960.

There are many American publications, all admirable in their own way as factual representations of public health practice in that country. The title of Dr. Hanlon's book, with its emphasis on the principles of administration, might be misleading because, although this forms the major part of the substance, the pattern on which this has been based is fascinating and attractive, it contains a wealth of information which would well repay the student, not only of public health in particular but of medical history in general.

A book of 686 text pages is often forbidding by its very size, but the description of the changing environmental pattern, with its new emphasis on the social pathology of the chronic diseases, mental health, accidents and other factors in this transitional period emphasizes all the more the importance of the increasing needs for the social services to work more closely with medical care. It demonstrates the part which public health administration and principles have to play in this approach. It is pleasing to read Dr. Hanlon's tribute to the English influence on the development of America's public health.

This is a readable book which is interesting and instructive and should form a welcome addition to any medical library.

The Principles and Practice of Medicine. Edited by Sir Stanley Davidson, B.A.Cantab., M.D., F.R.C.P.Edin., F.R.C.P.Lond., M.D.Oslo, F.R.S.Edin. 5th ed. (Pp. xi + 1112; illustrated. 35s.) Edinburgh and London: E. & S. Livingstone Ltd. 1960.

Five editions in eight years is sufficient testimony to the popularity of this book, and it is a popularity well merited. Although some 45 pages longer than the last edition, Sir Stanley and his henchmen have maintained the same excellent balance that is the hallmark of authoritative editorial control. No other textbook in the English language provides as much at so little cost and with so few mistakes. It is wholly admirable.

Clinical Physiology. Edited by E. J. M. Campbell, B.Sc., Ph.D., M.D., M.R.C.P., and C. J. Dickinson, B.A., B.Sc., B.M., M.R.C.P. (Pp. xi + 530; illustrated. 50s.) Oxford: Blackwell Scientific Publications Ltd. 1960.

Each chapter in this book is made up of four sections. The first two deal with normal and disordered function; the third is concerned with the physiological principles underlying the tests used in clinical practice, and the fourth is a summary showing how these tests are used in the diagnosis and management of the patient. The central nervous system is not considered but the rest of medicine is adequately covered.

The chapters vary somewhat in quality and in emphasis, and the different authors are not always writing for the same reader. Indeed the main difficulty is to decide for whom this book is written. It will not appeal to the physiologist; it is too advanced for the average medical student; and it is not sufficiently detailed in practical application for the registrar. Although the specialist may not be particularly interested in the chapter dealing with his own subject he will enjoy most of the others.

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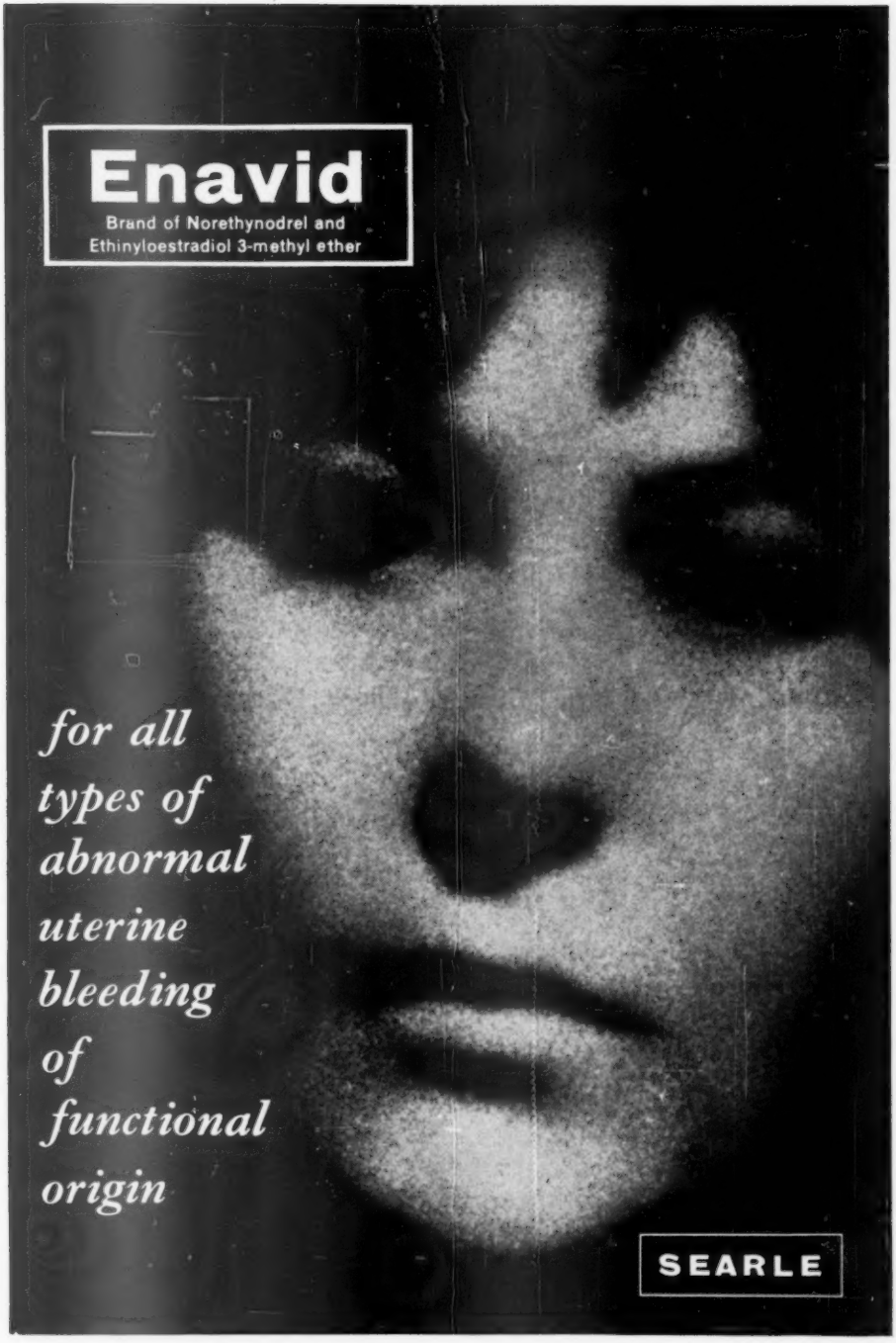
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